

U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

PB-267 981

Dietary Subacute Toxicity of Ethylene Thiourea in the Laboratory Rat

Battelle Columbus Labs, Ohio

Prepared for

Health Effects Research Lab, Research Triangle Park, N C

May 77

PB 267 981

EPA-600/1-77-023
May 1977

Environmental Health Effects Research Series

DIETARY SUBACUTE TOXICITY OF ETHYLENE THIOUREA IN THE LABORATORY RAT



REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22151

TECHNICAL REPORT DATA

(Please read Instructions found on the reverse before completing)

1. REPORT NO. EPA-600/1-77-023	3. RECIPIENT'S ACCESSION NO.
2. TITLE AND SUBTITLE DIETARY SUBSTRUCTURE TOXICITY OF ETHYLENE THIOUREA IN THE LABORATORY RAT	4. REPORT DATE May 1977
5. AUTHOR(S) Ralph I. Freudenthal	6. PERFORMING ORGANIZATION CODE
7. PERFORMING ORGANIZATION NAME AND ADDRESS Battelle Columbus Laboratories 505 King Avenue Columbus, Ohio 43201	8. PERFORMING ORGANIZATION REPORT NO.
9. SPONSORING AGENCY NAME AND ADDRESS Health Effects Research Laboratory Office of Research and Development U.S. Environmental Protection Agency Research Triangle Park, N.C. 27711	10. PROGRAM ELEMENT NO. 1E6616
11. CONTRACT/GRANT NO. 60-02-1716	12. TYPE OF REPORT AND PERIOD COVERED
13. SUPPLEMENTARY NOTES	14. SPONSORING AGENCY CODE EPA 600/11

15. ABSTRACT
Ethylene thiourea (ETU) was fed to groups of rats at 0, 1, 5, 25, 125 or 625 ppm for up to 90 days. Other groups of rats received either propylthiouracil (PTU; 125 ppm) or amiloride (50 ppm) in their diets as positive controls. Only those rats which received ETU at 125 or 625 ppm and those ingesting PTU or amiloride demonstrated a measurable toxic response. This toxicity was reflected as an alteration in thyroid function and a significant change in thyroid morphology. Ingestion of 625 ppm ETU or 125 ppm PTU resulted in very substantial decreases in serum triiodothyronine (T-3) and thyroxine (T-4). Marked increases in serum thyroid stimulating hormone (TSH) levels were found in the 625 and 125 ppm ETU rats, the 125 PTU rats and the rats receiving amiloride, at each time point this hormone was measured. A decrease in iodide uptake by the thyroid was also found in the rats ingesting 625 ppm ETU. While a statistically significant increase in serum T-4 and degree of thyroid hyperplasia was observed for the rats ingesting 25 ppm ETU for 60 days, normal thyroid hormone levels and thyroid morphology was found in the rats on 25 ppm ETU for either 30 or 90 days. Based on biochemical and microscopic changes examined, the no-effect level for dietary ETU in this 90-day study is considered to be 25 ppm, equivalent to an average intake ranging from 19.5 mg/kg body weight at Week 1 to 12.5 mg/kg body weight at Week 12.

17. KEY WORDS AND DOCUMENT ANALYSIS		
A. DESCRIPTORS thioureas toxicity toxic tolerances rats	B. IDENTIFIERS OPEN ENDED TERMS ethylene thiourea ETU	C. GDSAP Field Group 06, 1
18. DISTRIBUTION STATEMENT RELEASE TO PUM JC	19. SECURITY CLASSIFICATION UNCLASSIFIED 20. SECURITY CLASSIFICATION UNCLASSIFIED	21. NO. OF PAGES 86 22. PRICE \$1.00 - Acl

May 1977

DIETARY SUBACUTE TOXICITY OF
ETHYLENE THIOUREA IN THE
LABORATORY RAT

by

Ralph I. Freudenthal
Battelle Columbus Laboratories
305 King Avenue
Columbus, Ohio 43201

Contract No. 68-02-1715

Project Officer

Ronald L. Baron
Environmental Toxicology Division
Health Effects Research Laboratory
Research Triangle Park, N.C. 27711

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF RESEARCH AND DEVELOPMENT
HEALTH EFFECTS RESEARCH LABORATORY
RESEARCH TRIANGLE PARK, N.C. 27711

DISCLAIMER

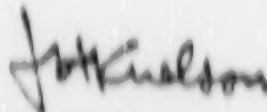
This report has been reviewed by the Health Effects Research Laboratory, U.S. Environmental Protection Agency, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the U.S. Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the relative risk of existing and new man-made environmental hazards is necessary for the establishment of sound regulatory policy. These regulations serve to enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our Nation's population.

The Health Effects Research Laboratory, Research Triangle Park, conducts a coordinated environmental health research program in toxicology, epidemiology, and clinical studies using human volunteer subjects. These studies address problems in air pollution, non-ionizing radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory develops and revises air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is preparing the health basis for non-ionizing radiation standards. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator to assure the adequacy of health care and surveillance of persons having suffered imminent and substantial endangerment of their health.

The significance of the occurrence of residues of pesticides or metabolites of pesticides in or on plants destined for human consumption must be considered with respect to its ultimate impact on human health. The present study evaluates the effect of the presence of ethylenethiourea (ETU) in the diet of a mammalian model test system. ETU is the major metabolite of a class of fungicides (ethylenedithiocarbamates) and the toxicological hazard associated with this biologically active metabolite as a residue in food is under intensive investigation. An evaluation of the health hazards associated with the presence of ETU in food includes the primary effects on the thyroid and liver as well as several associated biochemical parameters in an effort to determine a dietary level which might be safe for man.



John H. Enelson, M.D.
Director,
Health Effects Research Laboratory

ABSTRACT

Ethylene thiourea (ETU) was fed to groups of rats at 0, 1, 5, 25, 125 or 625 ppm for up to 90 days. Other groups of rats received either propylthiouracil (PTU; 125 ppm) or amitrone (30 ppm) in their diets as positive controls. Only those rats which received ETU at 125 or 625 ppm and those ingesting PTU or amitrone demonstrated a measurable toxic response. This toxicity was reflected as an alteration in thyroid function and a significant change in thyroid morphology.

Ingestion of 625 ppm ETU, or 125 ppm PTU resulted in very substantial decreases in serum triiodothyronine (T-3) and thyroxine (T-4). Marked increases in serum thyroid stimulating hormone (TSH) levels were found in the 625 and 125 ppm ETU rats, the 125 PTU rat and the rats receiving amitrone; at each time point this hormone was measured. A decrease in iodide uptake by the thyroid was also found in the rats which ingested 625 ppm ETU. While a statistically significant increase in serum T-4 and degree of thyroid hyperplasia was observed for the rats ingesting 25 ppm ETU for 60 days, normal thyroid hormone levels and thyroid morphology was found in the rats on 25 ppm ETU for either 30 or 90 days.

Based on biochemical and microscopic changes examined, the no-effect level for dietary ETU in this 90-day study is considered to be 25 ppm, equivalent to an average intake ranging from 19.5 mg/kg body weight at Week 1 to 13.5 mg/kg body weight at Week 12.

CONTENTS

Foreword	iii
Abstract	iv
Figures	vi
Tables	vii

Introduction	1
Experimental	2
Materials	2
STU Purity Analysis	2
Thyroid Function and Control	2
Evaluation of Test Kits	3
Methods	4
Results	5
References	9

FIGURES

<u>Number</u>		<u>Page</u>
1	MS Analysis of the ETU used as the test chemical	11
2	MS of the ETU used as the test chemical	12
3	Diet consumption	13
4	Test chemical consumption	14
5	Body weight gain	15

TABLE

Number		Page
1	ETU Protocol Design	16
2	Tissues Removed and Weighed During Necropsy	16
3	Thyroid Hormone Levels - After 30 Days on Study	17
4	Thyroid Hormone Levels - After 60 Days on Study	18
5	Thyroid Hormone Levels - After 90 Days on Study	19
6	Free Thyroxine Index	20
7	Weekly Diet Consumption	21
8	Weekly Test Chemical Ingestion	23
9	Weekly Body Weight Gain	24
10	Organ Weights Obtained at Necropsy	26
11	Organ Weight:Body Weight Ratio	28
12	Organ Weight:Brain Weight Ratio	32
13	Abnormal Changes Observed for Liver, Skin and Thyroid	36
14	Grading of Degree of Hyperplasia From Microscopic Appearance of the Thyroid Gland	37
15	Thyroid Hyperplasia Observed in ETU Test Animals	38
16	Changes in Thyroid Morphology in Rats Which Ingested 625 ppm ETU for Ninety Days	39

INTRODUCTION

The salts of ethylenedithiocarbamic acid (EDDC) have been extensively used against a variety of pathogenic plant fungi. A principal impurity and degradation product of the EDDC fungicides is ethylene thiourea (2-imidazolidinethione; ETU). ETU has been identified as an impurity in commercial EDDC formulations (1, 2). It has been reported to occur as a result of metabolic (3, 4, 5) and chemical (6, 7, 8) alterations of the commercial fungicides. ETU has been identified on a number of different crops which had been field-sprayed with a commercial formulation of EDDC (9, 10). Cooking of foods containing EDDC residues also results in the formation of ETU (11, 12).

Early studies evaluating the toxicity of the EDDC fungicides reported a major effect to be thyroid hyperplasia and neoplasia (13, 14, 15). The toxicity of ETU has also been studied and found to be essentially similar to that of the parent fungicide, producing thyroid neoplasia in rats (16, 17) and liver tumors in mice (14). In these published reports, recorded parameters consisted of body weights, organ weights, food consumption, ^{131}I uptake, and terminal histopathology. In the ETU subacute toxicity study reported herein, thyroid hormone level measurements were also made to determine at what dietary dose level ETU causes thyroid hormone alterations and to establish a dietary concentration which does not induce thyroid changes leading to hyperplasia. In addition, it was hoped that a relationship between altered thyroid hormone levels and thyroid hyperplasia could be established.

EXPERIMENTAL

Materials

Sprague Dawley-derived rats were purchased from Charles River Laboratories (Wilmington, Massachusetts). ETU (estimated to be >95 percent pure) was obtained from the Aldrich Chemical Company (Milwaukee, Wisconsin), and propylthiouracil (PTU) and amiloride (3-amino-1,2,4-triazole) were purchased from the Sigma Chemical Company (St. Louis, Missouri). ^{125}I for the thyroid iodine uptake studies was obtained from New England Nuclear (Boston, Massachusetts). Commercial test kits for measuring serum thyroxine (T-4) and thyroid binding globulin (TBG) were purchased from Nuclear Medical Laboratories, Inc. (Dallas, Texas). Triiodothyronine (T-3) kits were obtained from Diagnostic Products Corporation (Los Angeles, California). Initial serum TSH measurements were performed with kits purchased from Beckman Instruments, Inc. (Fullerton, California). Shortly after this study began, the specificity of the antiserum for human TSH was changed and the measure of rat TSH was no longer accomplished.

TSH kits from ICN Medical, Pharmacia Diagnostics and Calbiochem were purchased and evaluated as possible substitutes for measuring rat TSH. Only the Calbiochem TSH RIA kit proved suitable, and it was used at the end of this study. TSH was not measured during most of the study.

ETU Purity Analysis

The ETU used in this study was analyzed by mass spectroscopy and nuclear magnetic resonance spectrometry (NMR). Direct probe high resolution mass spectroscopy showed a strong parent ion at m/e 101. This is shown in Figures 1 and 2. It was estimated through the use of both ^{13}C and ^2H NMR spectroscopy that ETU was 96.8 percent pure.

Thyroid Function and Control

Thyroid hormone is biosynthesized in the thyroid gland by the iodination of tyrosine. Iodotyrosines are coupled to form T-3 and T-4. These active hormones are released into the bloodstream and are distributed throughout the body where they regulate metabolic processes. Hormone synthesis and release is controlled by a peptide which originates in the anterior lobe of the pituitary, the thyroid stimulating hormone

(TSH). Pituitary secretion of TSH is, in turn, regulated by two factors, a hormone released by the hypothalamus called thyrotropin releasing hormone (TRH), and the concentration of free thyroid hormones (T-3 and T-4) in the interstitial fluid which bathes both the pituitary and hypothalamus.

Increased serum thyroid hormone concentrations suppress secretion of TSH while decreased hormone levels augment TSH release, providing for a steady-state thyroid hormone concentration. Recent studies indicate that thyroid hormone blocks pituitary response to TRH. As the serum levels of T-3 and T-4 fall below a threshold concentration, the TSH-secreting cells of the anterior pituitary become responsive to TRH and secrete TSH which, in turn, raises serum thyroid hormone levels. This feedback control system is designed to provide a constant supply of thyroid hormone to peripheral tissues, where it acts as a regulator of cellular metabolism.

Chemical substances that impair the synthesis or release of thyroid hormone cause hyperplasia of the thyroid gland. Continued exposure to antithyroid chemicals results in the transformation of the hyperplastic tissue to a malignant form. It is now well documented that chemicals altering thyroid function can initiate thyroid neoplasia (18, 19). Chemicals which impair the synthesis or release of TSH from the pituitary can severely affect the feedback control system which regulates serum T-3 and T-4 levels.

In summary, altered thyroid function can result from the action of a chemical on iodine uptake and incorporation, synthesis or release of thyroid hormones, synthesis or release of TSH, or inactivation of receptors activated by either TSH (at the level of the thyroid) or by thyroid hormone (at the pituitary level). Using commercially available test kits, the serum concentration of T-3, T-4, TBO and TSH can be measured. ^{125}I uptake can be measured directly. The Free Thyroxine Index (FTI) was calculated and is reported for each group. The FTI is a measurement of free serum T-4. While the T-4 level, measured by the T-4 radioimmunoassay kit, is influenced by TBO concentrations, the FTI is a measurement of the amount of T-4 free in the serum, independent of the serum TBO concentration. The formula used to calculate the FTI is shown below:

$$\text{FTI} = \frac{(\text{T-4 } \text{f Bound})}{100} \times \text{T-4 ug/l}$$

Evaluation of Test Kits

We have previously shown that certain chemically induced alterations in thyroid function in rats could be measured using commercially available kits. We reported serum T-4 and TBO (T-3 binding) levels and ^{125}I uptake by the thyroid (20). Prior to the initiation of this ETU subacute

toxicity bioassay, we evaluated a new T-3 kit produced by Diagnostic Products Corporation (Los Angeles, California), and a TSH kit from Beckman Instruments (Fullerton, California). The T-3 diagnostic kit quantitatively measures total serum T-3 by radioimmunoassay. One hundred microliters of each serum sample (or standard) is mixed with an equal volume of ^{125}I labeled T-3. Upon addition of the T-3 specific antibody, the endogenous serum T-3 and the radioactive T-3 compete for binding sites. This reaction takes place in the presence of ANS (anion=8-octilino=1-naphthalene sulfonic acid) which blocks the interaction of T-3 with other serum proteins. A second antibody, goat anti/rabbit gamma globulin, is added to separate the free serum T-3 from the bound T-3. This solution is well mixed and incubated at 37°C for 15 minutes. An ice cold solution of 6 percent polyethylene glycol is then added to help precipitate the antibody bound T-3. Following centrifugation (1,500mg; 20 min.), the supernatant containing the free T-3 is decanted and the antibody bound T-3 precipitant is counted. A five point standard curve is constructed and serum T-3 levels are determined from this curve.

The Beckman TSH diagnostic kit quantitatively measures total serum TSH by radioimmunoassay. The procedure is similar to that described above for the T-3 test. Serum from rats pretreated with amitrole was evaluated for T-3 and TSH levels and this was compared to values obtained from control serum.

Unfortunately, after the ETU subacute toxicity study began, Beckman switched to a new antiserum with increased specificity for human TSH. This kit would no longer measure rat TSH. Therefore, TSH kits from other commercial sources were purchased and evaluated as possible alternates. The kit produced by Calbiochem contains a relatively nonspecific TSH antiserum and will measure rat serum TSH levels. Unfortunately, this was not confirmed until near the end of the study and for this reason, TSH values are available for only very few groups.

Methods

ETU, PTU, or amitrole was added to corn oil and then incorporated into powdered rodent feed⁽¹⁾ using a twin shell tumble blender. The final corn-oil concentration in the blended feed was 1 percent. The test diets were prepared fresh weekly. The dietary levels of ETU were 625, 125, 25, 5 and 1 ppm, PTU was 125 ppm and amitrole, 50 ppm. These dietary levels of PTU and amitrole were previously shown to produce significant antithyroid effects (21, 22). A control group received powdered diet containing 1 percent corn oil. Each of the seven dosage groups contained 60 male and 60 female rats. The control group contained 72 male and 72 female rats. The animals were placed on study as outlined in Table 1.

(1) Ralston Purina Company, Richmond, Indiana.

At 30-day intervals, 10 rats of each sex from each test group were sacrificed and serum T-3, T-4, TBO and TSH concentrations were measured. These rats were also used for necropsy. The remaining 10 rats of each sex per group were used for thyroid ¹²⁵I uptake studies. Each rat was individually caged throughout the study. Body weight and food consumption was determined weekly. Each rat was toe-punched at the start of the study for permanent identification.

The 10 tissues removed during necropsy are listed in Table 2. Due to excessive salivation and abnormal skin-hair coat development at the 625 ppm ETU level, skin and mandibular salivary glands were also removed during necropsy from the rats which received the high diet. The thyroid gland and liver were examined microscopically in all study groups. These two tissues were fixed in formalin imbedded in paraffin, sectioned (6 microns) and stained with Hematoxylin-Eosin. The remaining tissues were stored in 10 percent buffered formalin.

RESULTS

The rats which received 625 ppm ETU showed clinical signs of poisoning by the eighth day on study. Excessive salivation, loss of hair or failure to replace normal hair loss, rough and bristly hair coat, and scaly skin texture was observed. Ingestion of ETU was calculated and found to range from 11.7 to 15.2 mg/day in female rats to from 13.0 to 17.3 mg/day in male rats. Table 3 shows data on the weekly consumption of ETU and other chemicals by all animals on study. Fourteen of the 40 rats on the 625 ppm ETU 60-day study died between days 40 and 50 of the study. Only one rat from the 90-day group died.

The rats receiving 125, 25, 5 and 1 ppm ETU, control diet, 50 ppm amitrole or 125 ppm PTU showed no adverse clinical effects.

Consistent with the observable clinical changes, several biochemical changes were noted. Rats ingesting ETU at 625 ppm showed a significant decrease in iodine uptake. The percent T-3 bound to TBO was lower than normal at the 30- and 90-day evaluations. Serum concentrations of T-3 and T-4 were also very substantially lower than the levels obtained for the control rats. The serum TSH concentration for the 625 ppm rats, measured only at the time of the 30-day evaluation, was increased to more than twice the serum TSH concentration observed for the control rats. Significant differences in free T-4 were also found, as determined by the FTI.

The rats of iodine uptake, the percentage of T-3 bound to TBO, and the serum T-3 concentration in the rats receiving 125 ppm ETU were not significantly different from the control group. However, a statistically significant decrease in total serum T-4 concentration and in free serum

T-4 measured at the 30-, 60- and 90-day evaluations was observed. The serum TSH concentration in the 125 ppm ETU rats at 30 days was approximately three times the concentration measured in the control rats.

With one exception, there were no significant measurable differences in iodine uptake, T-3 binding to TBG or serum T-3, T-4 and TSH levels in the rats receiving ETU at either 25, 5 or 1 ppm for 30, 60 or 90 days. The rats ingesting 25 ppm ETU for 60 days showed a statistically significant increase in serum T-4 concentration. This was not evident at 30 or 90 days.

After 30 days of amitrole ingestion, very significantly decreased serum T-3 and T-4 levels were observed. The female rats from this group also had a decreased percent of T-3 bound to TBG. Both the male and female rats had an increased serum TSH concentration. In a previous report (EHS toxicity study), we showed that ingestion of 50 ppm amitrole for four days resulted in a significant decrease in iodine uptake and T-4 serum concentrations. While the decreased T-4 levels are still found after 30 days of amitrole ingestion, iodine uptake appears to have returned to normal, probably as a result of biological compensation. At 60 and 90 days, normal values for all of the thyroid function measurements were noted.

The rats which received PTU had decreased serum T-3 and T-4 concentrations at 30, 60, and 90 days. The serum TBG level was affected only in the 60- and 90-day test groups. Since the PTU study was added after the ETU study had started, TSH values were obtainable for the 60- and 90-day PTU test groups. Both groups had markedly elevated serum TSH levels.

Tables 3, 4 and 5 list the percent iodine uptake, TBG, T-3 and T-4 concentrations after 30, 60 and 90 days on study, respectively. Also included in these tables are the values for the amitrole and PTU positive controls. TSH values are given for those test groups in which it was measured. The calculated FTI for each test group is shown in Table 6.

Diet consumption for all groups is shown in Figure 3. With the exception of those rats receiving 625 ppm ETU and those ingesting 125 PTU, there was no significant difference in feed consumption. A 30 percent to 40 percent reduction in food consumption was observed in the rats on the 625 ppm ETU and 125 ppm PTU test diets, compared to control animal consumption levels. The average weekly feed consumption for each test group with the standard deviation is listed in Table 7.

The amount of ETU, PTU or amitrole consumed per week is shown in Figure 4. The average amount of each test chemical consumed along with the standard deviation is listed in Table 8.

Individual body weights were recorded weekly throughout the study. Table 9 summarizes the body weight data (group mean $\pm$ S.D.). Figure 5 shows the weekly body weight gain for each dietary level. Only those rats which receive 625 ppm ETU or 125 ppm PTU test diets showed a marked decrease in body weight gain. No difference in body weight gain was observed for those rats which received ETU at 125, 25, 5 or 1 ppm, or amitrole, as compared to the control group.

At the conclusion of the study, gross necropsies were performed and certain organs were removed and weighed (see Table 2). Table 10 lists the mean organ weights and standard deviation for each group. There were no significant differences in organ weights in those rats fed 25, 5, 1 and 0 ppm ETU. However, thyroid hyperplasia was observed in all animals which received 625 and 125 ppm ETU, 125 ppm PTU or 50 ppm amitrole in their diet for 30, 60 or 90 days.

The organ-weight-to-body-weight ratios were calculated (Table 11). The spleen-to-body-weight ratio for the rats which ingested 625 ppm ETU is significantly decreased while the ratios for the thyroid, brain, kidneys, testicles and pituitary are significantly higher than the corresponding control values. Increased thyroid-to-body-weight ratios were also found for the rats which received 125 ppm PTU, 50 ppm amitrole or 125 ppm ETU (Table 11).

Organ-weight-to-brain-weight ratios were also calculated (Table 12). No significant differences were found between rats receiving 125, 25, 5, 1 and 0 ppm ETU. For those rats ingesting 625 ppm ETU, the ratio of heart, spleen, kidney, adrenals (female) and ovaries-to-brain-weight was significantly decreased and the thyroid-to-brain-weight ratio was significantly increased compared to control values. The thyroid-to-brain-weight ratios in the rats which received 125 ppm ETU were also significantly increased in size at 30, 60 and 90 days.

An increased thyroid-to-brain-weight ratio was the only significant organ-to-brain-weight ratio change found in the 50 ppm amitrole test animals. The animals which received 125 ppm PTU for 30, 60 or 90 days showed a very significant decrease in organ-to-brain-weight ratios for heart, spleen, kidney, ovary, liver and adrenals. These animals had a very significant increase in thyroid-to-brain-weight ratios compared to the control values. The organ-weight-to-brain-weight ratios for the rats which received amitrole and PTU are listed in Table 12.

Gross examinations revealed the majority of the rats which received ETU at 125 or 625 ppm, as well as those animals which received PTU or amitrole for 30, 60 or 90 days had enlarged red thyroids. Grossly visible patterns of centrilobular congestion were present in a few random rats fed amitrole or ETU. A summary of gross changes is presented in Table 13.

Microscopic examination of tissues was restricted to thyroid and liver. The thyroids were graded for degree of hyperplasia using a slight modification of the procedure of Astwood (23), and as defined in Table 14. Varying degrees of thyroid microfollicular hyperplasia resulted at feeding levels of ETU above 25 ppm (Table 15). Relatively mild changes were noted in animals fed 125 ppm ETU for 30 days as compared to the moderate changes observed in the rats fed 625 ppm ETU for the same time period. Marked thyroid microfollicular hyperplasia and reduced colloid formation were found in animals fed amitrile or PTU for 30 days. At 60 days, the rats receiving the three highest levels of ETU (625, 125 and 30 ppm) and the amitrile treatment group showed moderate thyroid hyperplasia as compared to the 60-day PTU group which was more marked in its thyroid hyperplastic response and reduced colloid production.

Ninety days of dietary exposure to 625 ppm ETU also resulted in microfollicular hyperplasia but not as severe as seen with PTU in the same time period. Numerous changes ranging from adenomatous hyperplasia of follicles to what appear to be true solid adenomas were present in the thyroids in the 625 ppm ETU group. Table 16 categorizes the hyperplastic thyroids from the 625 ppm ETU test group into either solid adenomas, cystic adenomas, adenomatous changes or cystic-like follicles. No adenomas were observed in the thyroid sections taken from the other dietary groups. No liver tumors were observed in the rats at any dosage level of ETU or in those animals which received PTU or amitrile. The majority of the livers examined microscopically had mild centrilobular changes which can be described as follows. Portal triad areas have a smooth sheet of hepatocytes cut relatively across the nucleus and cytoplasm at about the same level giving well defined cell boundaries and cytoplasmic proportions. As one approaches the mid-portal area and progresses into the centrilobular area of small central veins, the pattern changes to less distinct cell borders of swollen cytoplasmic material with fewer apparent nuclei. The chord pattern is less distinct and there is a mild increase in small polyploid nuclei. The general appearance is that of increased cytoplasm, fewer nuclei and less orderly hepatic chords.

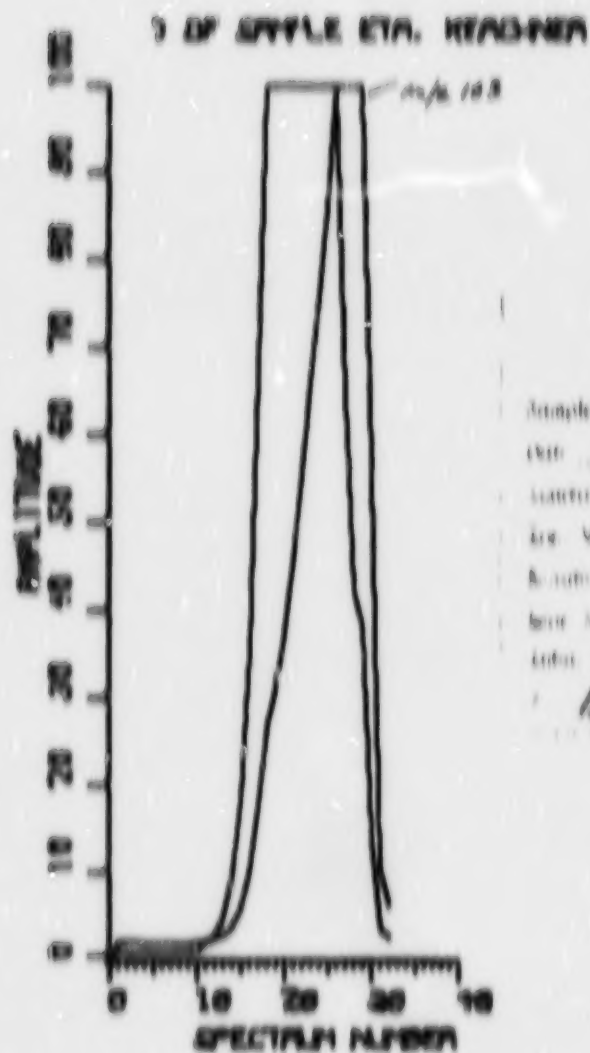
The data presented in this report show no significant measurable adverse effects of dietary ETU at dosages of 5 ppm and below. Significant toxic responses, observed as altered thyroid function and changes in thyroid morphology, resulted from the ingestion of ETU at 125 ppm or 625 ppm for 30, 60 or 90 days. The observable effects at 25 ppm were noted only at the 60-day interval and were not seen at 30 or 90 days. Based on these data, a dietary no-effect level in rats might be expected to be 25 ppm over the 90-day study.

REFERENCES

1. Clarke, D. C., Baum, R., Stanley, E. L. and Hester, W. F., *Anal. Chem.* 23, 1842-1844 (1951).
2. Bontuyan, M. R., Locker, L. B., Kaiser, T. E., Giang, F., and Olive, R. M., Survey of Ethylene Thiourea in Commercial Ethylene Bis Dithiocarbamate Formulations, *J. Assoc. Off. Anal. Chem.* 55, 923-925 (1972).
3. Engst, R. and Schnaak, W., Investigations of the Metabolism of Fungicidal Ethylene Bisdithiocarbamates Maneb and Zineb, *B. Lebensmittel, Guters, Forsch.* 136, 216-221 (1967).
4. Seidler, H., Gierzig, M., Schnaak, W. and Engst, R., Metabolism of certain insecticides and fungicides in the Rat, *Nahrung* 14, 363, 373 (1970).
5. Truhaut, R., Fujita, H., Lich, H. P. and Chaigneau, H., *Compt. Rend. Serie D.* 276, 229-233 (1973).
6. Lopatecki, L. E. and Newton, W., The Decomposition of Dithiocarbamate Fungicides with Special Reference to the Volatile Products, *Can. J. Bot.* 30, 131-138 (1952).
7. Fishbein, L. and Fawkes, J., Thin-layer Chromatography of Metallic Derivatives of Ethylene Bisdithiocarbamic Acid and Their Degradation Products, *J. Chromatogr.* 19, 364-369 (1965).
8. Engst, R. and Schnaak, W., Residues of Dithiocarbamate Fungicides and the Metabolites on Plant Foods, *Residue Rev.* 32, 45-67 (1974).
9. Yip, G., Onley, J. H., and Howard, S. F., Residues of Maneb and Ethylene Thiourea on Field-Sprayed Lettuce and Kale, *J. Assoc. Off. Anal. Chem.* 54, 1373-1375 (1971).
10. Newsome, W. H., Determination of Ethylene Thiourea Residues in Apples, *J. Agric. Food Chem.* 20, 967-969 (1972).
11. Newsome, W. H. and Laver, G. W., Effects of Roiling on the Formation of Ethylene Thiourea in Zineb Treated Food, *Bull. Environ. Contam. Toxicol.* 10, 151-154 (1973).
12. Watts, R. R., Stroherr, R. W. and Onley, J. H., Effects of Cooking on Ethylene Bisdithiocarbamate Degradation to Ethylene Thiourea, *Bull. Environ. Contam. Toxicol.* 12, 224-228 (1974).
13. Blackwell-Smith, R., Finnegan, J. E., Larsen, C. G., Sahyoun, P. F., Dreyfuss, M. L. and Haag, H. R., Toxicological Studies on Zinc and Disodium Ethylene Bisdithiocarbamates, *J. Pharmacol. Exp. Ther.* 109, 159-166 (1953).

REFERENCES (Continued)

14. Innes, J. R. M., Valerio, M., Ulland, B. M., Pailotta, A. J., Petrucelli, L., Fishbein, L., Hart, E. R., Falk, H. L., Klein, H., and Peters, A. J., Bioassay of Pesticides and Industrial Chemicals for Tumorigenicity in Mice. *J. Natl. Cancer Inst.* 32, 1101-1109 (1969).
15. Andrianova, M. M. and Alekseev, I. V., Carcinogenic Properties of the Pesticides Sovin, Maneb, Siram and Zineb. *Vopr. Pitan.* 29, 71-74 (1970).
16. Ulland, B. M., Weisburger, T. H., Weisburger, E. K., Rice, J. M., and Cypher, R., Thyroid Cancer in Rats From Ethylene Thiourea. *J. Natl. Cancer Inst.* 39, 683-684 (1972).
17. Graham, S. L., Davis, E. J., Hanson, W. H., and Graham, C. H., Effects of Prolonged Ethylene Thiourea Ingestion on the Thyroid of the Rat. *Fd. Cosmet. Toxicol.* 13, 493-499 (1975).
18. Jukes, T. H. and Shaffer, G. B., Antithyroid Effects of Aminotriazole. *Science* 132, 296-297 (1960).
19. Purves, H. D., and Grisham, W. E., Thyroid Tumors in Rats Treated with Thiourea. *Br. J. Exp. Path.* 28, 46-53 (1947).
20. Freudenthal, R. I., Kerchner, G. A., Persing, R. L., Baumel, I., and Baron, R. L., Subacute Toxicity of Ethylene-bis(isothiocyanate) Sulfide in the Laboratory Rat. *J. Toxicol. Environ. Health*, In Press.
21. Griessen, M. and Lemarchand-Beraud, T., Thyrotropin Secretion and Metabolism in Rats during Propylthiouracil Treatment. *Endocrinol.* 92, 166-173 (1973).
22. Seifter, J. and Ehrlich, W. E., Goitrogenic Compounds: Pharmacological and Pathological Effects. 92, 303-314 (1948).
23. Astwood, E. B., The Chemical Nature of Compounds Which Inhibit the Function of the Thyroid Gland. *J. Pharmacol. Exp. Ther.* 78, 79-82 (1943).



ANALYSIS OF THE ETU USED AS THE TEST CHEMICAL

Sample: 4.16/76 Total: OC (Unit: 1)

Date: 4.16/76 Remarks: Adap

Location: 0 Method: in bit

Amplitude: 10⁻⁶ Frequency: 1000 Hz

Wave: 10⁻⁶ Amplitude: 16 (Unit: 1)

Wave: 10⁻⁶ Wave: 1000 Material: Adap

Unit: 1 Wave: OC Wave: 1000

Wave: 1000 Wave: 1000 Wave: 1000

FIGURE 1. MS ANALYSIS OF THE ETU USED AS THE TEST CHEMICAL

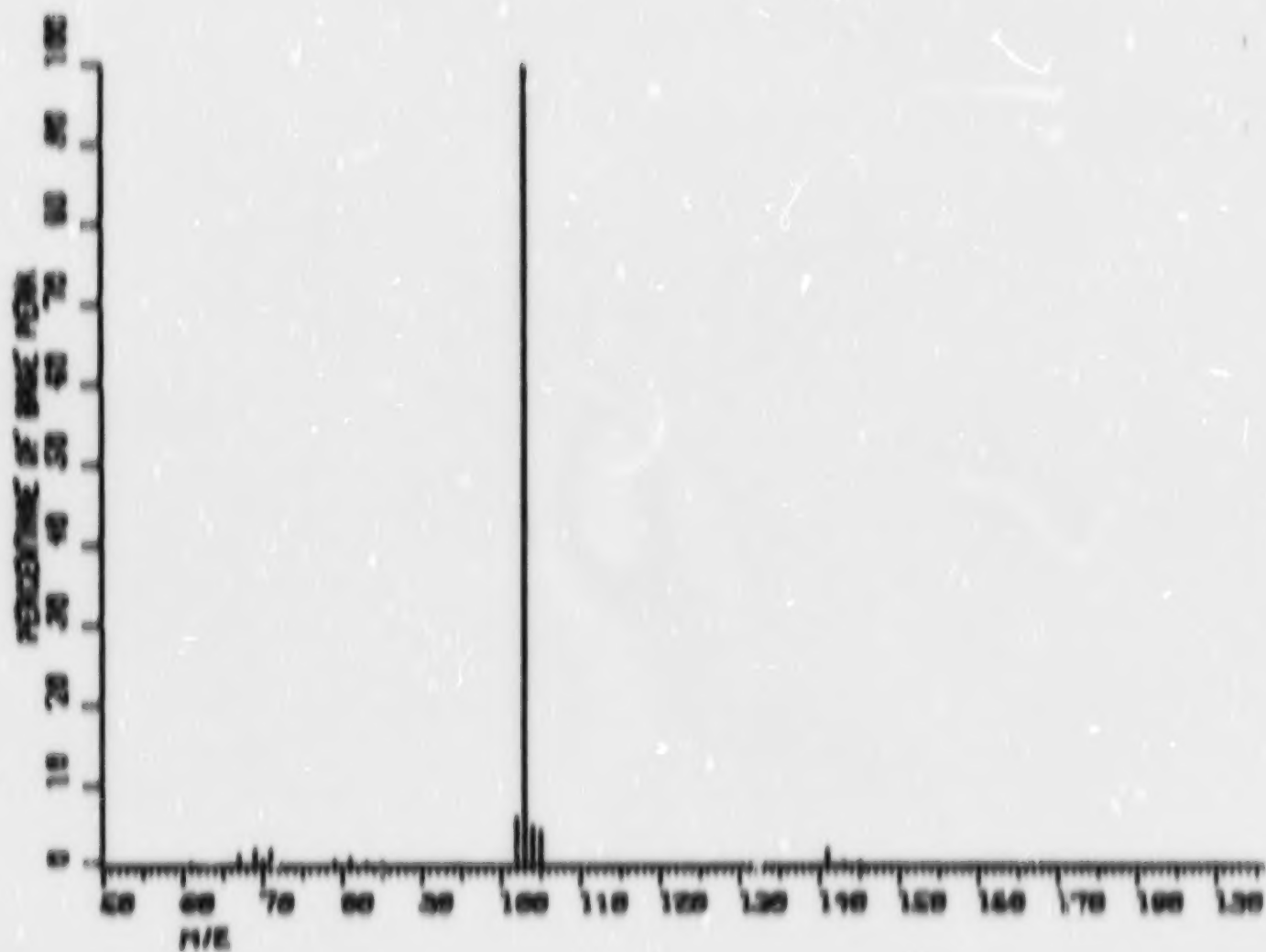


FIGURE 2. MS OF THE ETU USED AS THE TEST CHEMICAL

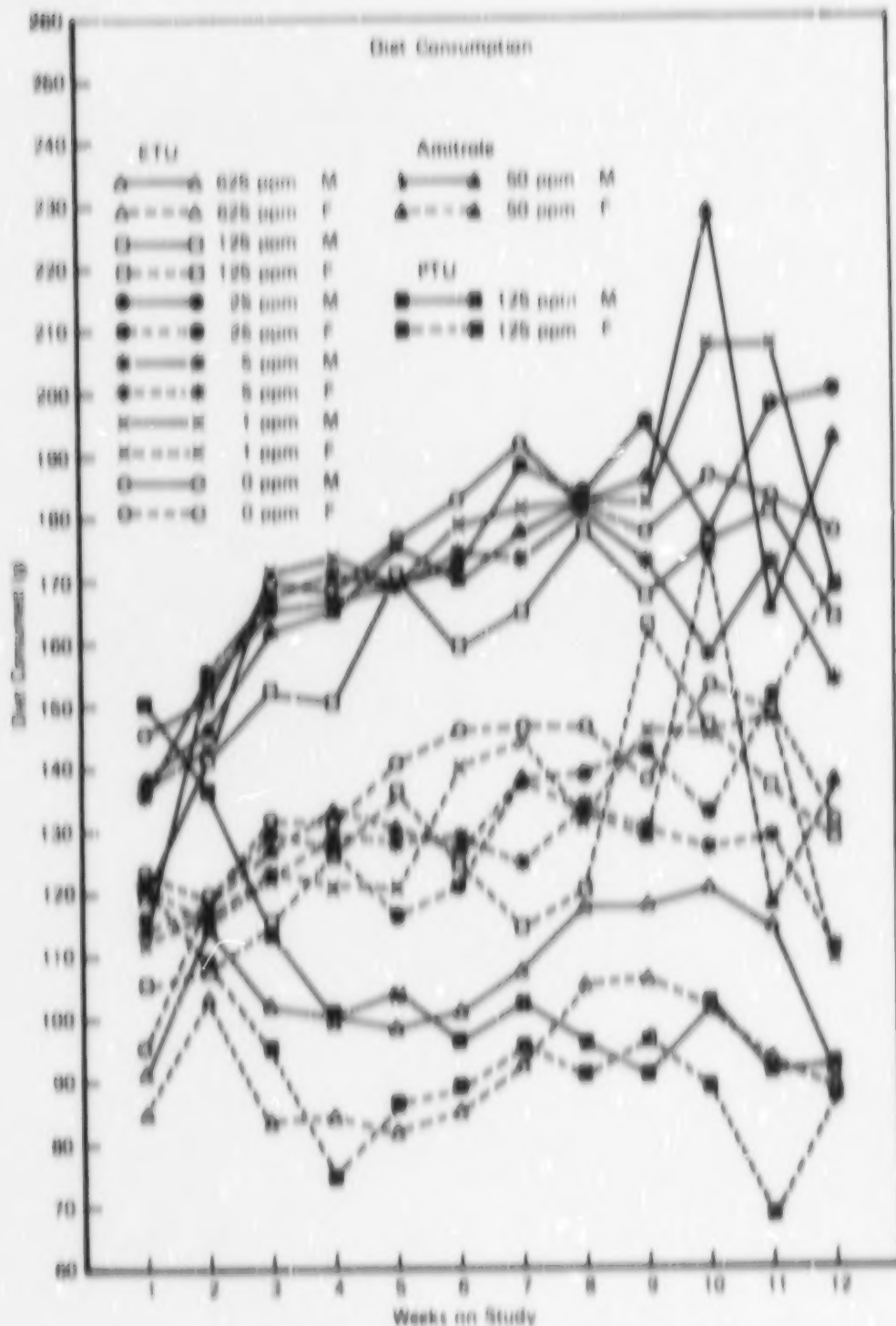


FIGURE 1. DIET CONSUMPTION

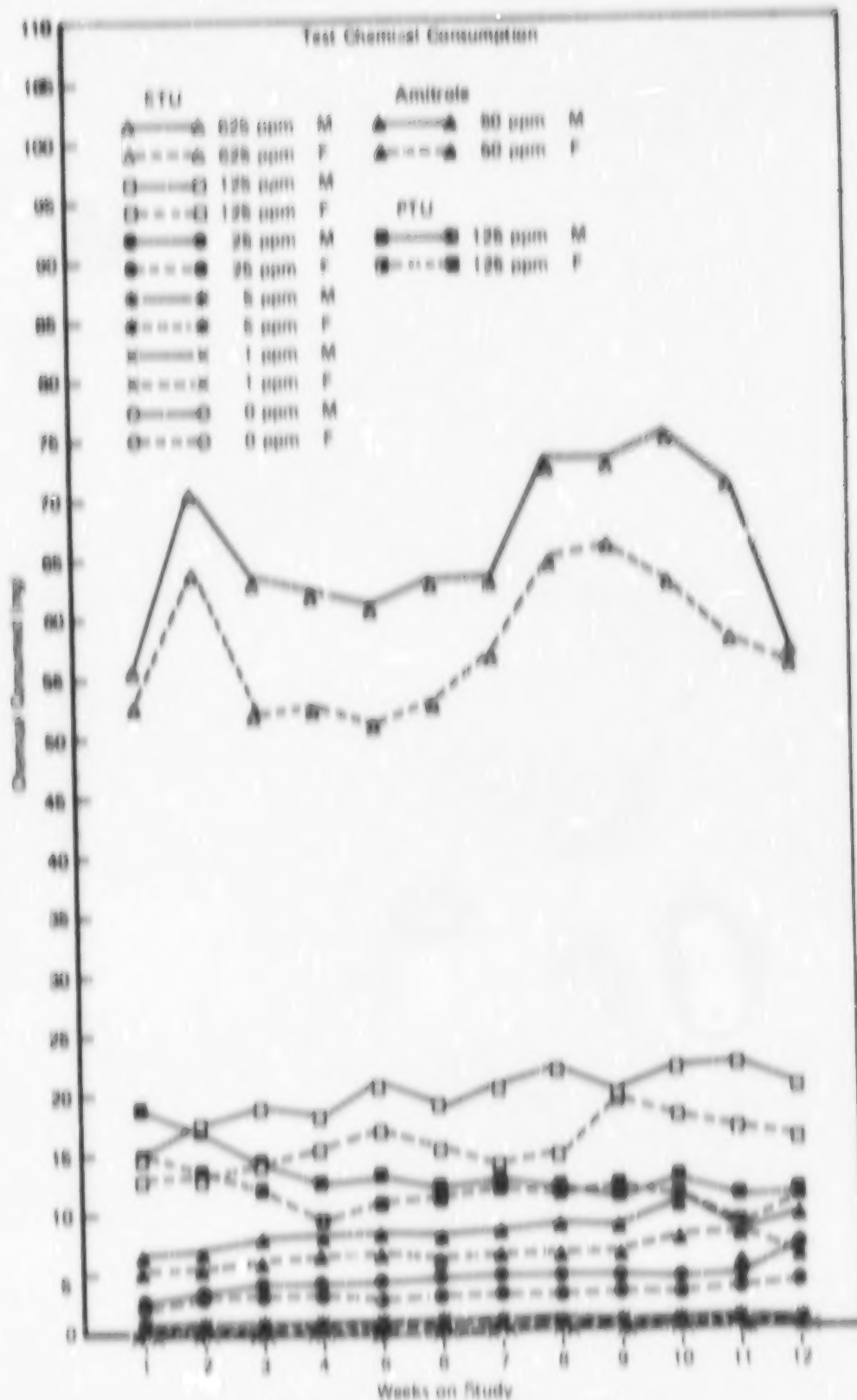


FIGURE 4. TEST CHEMICAL CONSUMPTION

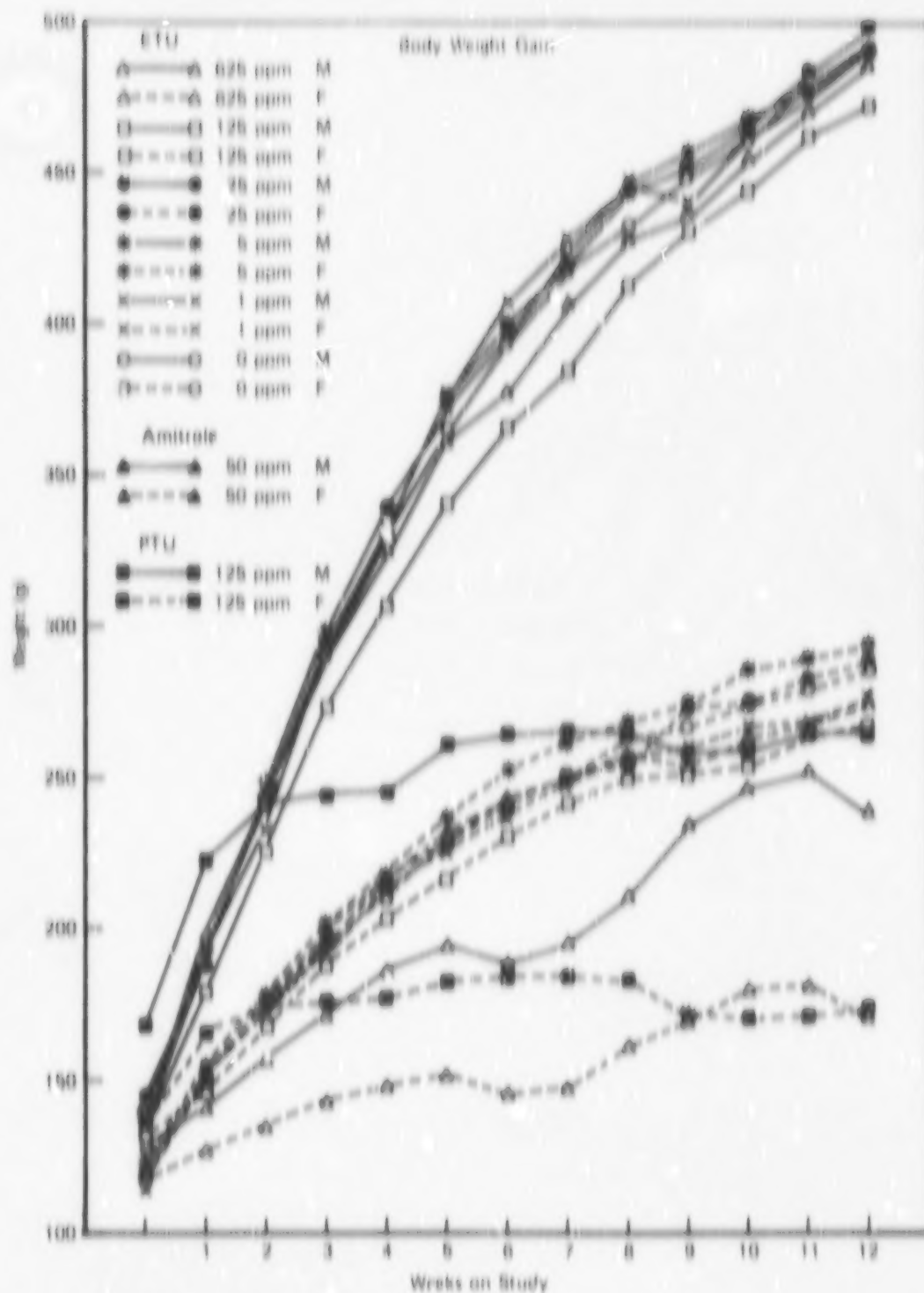


FIGURE 5. BODY WEIGHT GAIN

TABLE 1. ETU PROTOCOL DESIGN

ETU (ppm)	Sex	Number of Rats/Treatment Period		
		30 Days	60 Days	90 Days
625	M	20	20	20
625	F	20	20	20
125	M	20	20	20
125	F	20	20	20
25	M	20	20	20
25	F	20	20	20
5	M	20	20	20
5	F	20	20	20
1	M	20	20	20
1	F	20	20	20
0	M	24	24	24
0	F	24	24	24
Amikacin				
(ppm)				
50	M	20	20	20
50	F	20	20	20
PTU				
(ppm)				
125	M	20	20	20
125	F	20	20	20

TABLE 2. TISSUES REMOVED AND WEIGHED DURING NECROPSY

Heart	*Liver
Spleen	Pituitary
Kidney	*Thyroid (paired)
Ovary (paired)	Adrenal (paired)
Testicle (paired)	Brain

* Tissues processed for histopathologic evaluation.

TABLE 3. THYROID HORMONE LEVELS - AFTER 30 DAYS ON STUDY

ETU (ppm)	Sex	125 I (percent uptake)	TBG (percent T-3 bound)	T-3 (ng percent)	T-4 (ng percent)	TSH (mIU per ml)
625	M	1.3 ± 0.4*	60.3 ± 2.6*	57.3 ± 3.7*	0.9 ± 0.6*	14.3 ± 0.9*
625	F	3.1 ± 1.4*	60.6 ± 1.8*	58.4 ± 9.9*	1.1 ± 1.0*	14.6 ± 1.9*
125	M	3.6 ± 0.8	62.7 ± 1.3*	71.1 ± 11.8*	2.6 ± 0.4*	23.3 ± 5.9*
125	F	4.0 ± 1.7	61.5 ± 1.3*	104.4 ± 16.3*	2.1 ± 0.5*	18.3 ± 4.0*
25	M	2.9 ± 0.6	65.7 ± 0.3	67.1 ± 15.9	5.6 ± 1.1	7.3 ± 1.5
25	F	3.2 ± 1.3	63.5 ± 2.0	86.3 ± 14.8	3.8 ± 0.8	5.1 ± 1.3
5	M	3.6 ± 0.6	69.3 ± 6.3	79.0 ± 8.1	4.7 ± 0.4	6.7 ± 1.4
5	F	3.8 ± 1.0	68.9 ± 1.3	88.1 ± 12.8	2.9 ± 0.9	4.9 ± 1.4
1	M	3.7 ± 0.7	64.5 ± 1.2	82.1 ± 13.0	5.1 ± 1.0	6.4 ± 0.8
1	F	3.0 ± 0.5	63.4 ± 1.3	90.9 ± 11.3	3.5 ± 1.0	4.5 ± 0.9
0	M	3.6 ± 0.9	68.0 ± 3.6	76.0 ± 11.8	5.0 ± 1.7	6.7 ± 2.5
0	F	3.5 ± 0.9	66.0 ± 5.2	83.2 ± 16.2	3.8 ± 1.4	6.0 ± 4.1
Amterole						
(ppm)						
50	M	3.7 ± 3.1	63.0 ± 1.5	49.1 ± 19.5*	0.6 ± 0.8*	9.3 ± 0.6*
50	F	5.0 ± 3.5	61.4 ± 1.0*	55.2 ± 7.2	0.3 ± 0.3	8.9 ± 0.6
PTU						
(ppm)						
125	M	2.9 ± 1.1	67.8 ± 2.0	58.9 ± 6.1*	0.9 ± 0.2*	-
125	F	3.3 ± 0.7	69.5 ± 1.6	52.0 ± 8.0	0.7 ± 0.1	-

*Significantly different ($p < 0.05$) from corresponding control. Student's t test was used to make comparison between the control and treated animals. All data reported as the mean, ± S.D.

TABLE 4. THYROID HORMONE LEVELS - AFTER 60 DAYS ON STUDY

ETU (ppm)	Sex	¹²⁵ I (percent uptake)	TBQ (percent bound)	T-3 (ng Percent)	T-4 (ug percent)	TSH (μIU per ml)
625	M	1.9 ± 1.0*	79.0 ± 0.9	56.9 ± 10.3*	0.2 ± 0.1*	=
625	F	2.4 ± 1.8*	71.8 ± 1.4	56.8 ± 6.9*	0.2 ± 0.1*	=
125	M	3.6 ± 1.4	66.3 ± 1.3	79.8 ± 28.1	2.8 ± 0.5*	=
125	F	3.3 ± 1.0	66.3 ± 2.1	78.5 ± 25.6*	2.0 ± 0.5*	=
25	M	3.2 ± 0.7	76.9 ± 1.6	86.4 ± 7.6	2.8 ± 0.5*	=
25	F	3.7 ± 1.3	74.7 ± 1.7	126.2 ± 15.1	2.6 ± 0.5*	=
5	M	3.5 ± 0.8	66.4 ± 1.2	85.4 ± 12.7	4.9 ± 0.5	=
5	F	4.0 ± 0.8	64.0 ± 1.8	118.2 ± 16.3	2.9 ± 0.9	=
1	M	2.7 ± 0.6	70.4 ± 1.2	80.3 ± 12.0	4.9 ± 0.7	=
1	F	3.2 ± 0.7	67.1 ± 1.3	93.3 ± 13.5	2.8 ± 0.8	=
0	M	4.3 ± 0.9	73.6 ± 4.9	77.3 ± 0.5	4.8 ± 0.7	5.8 ± 0.4**
0	F	3.5 ± 0.8	69.4 ± 4.3	103.8 ± 19.1	3.3 ± 0.5	6.4 ± 0.9**

Amityole
(ppm)

50	M	4.0 ± 0.7	74.8 ± 1.6	83.4 ± 8.9	5.9 ± 0.8	=
50	F	4.8 ± 0.9	69.8 ± 1.3	111.6 ± 10.7	3.5 ± 0.6	=

PTU
(ppm)

125	M	3.9 ± 1.6	61.7 ± 2.6*	46.1 ± 3.9*	1.2 ± 0.2*	9.8 ± 1.0*
125	F	5.4 ± 1.7	62.2 ± 2.1*	50.9 ± 9.7*	0.8 ± 0.1*	10.8 ± 1.9*

* Significantly different (p < 0.05) from corresponding control.

** TSH values to be used as control for PTU group.

TABLE 5. THYROID HORMONE LEVELS - AFTER 90 DAYS ON STUDY

ETU (ppm)	Sex	125 I (percent uptake)	TBG (percent T-3 bound)	T-3 (ng percent)	T-4 (ng percent)	TSH (uIU per ml)
625	M	2.3 ± 0.8 ^a	62.7 ± 2.0 ^a	27.9 ± 13.3 ^a	1.1 ± 0.6 ^a	-
625	F	3.7 ± 1.8	63.7 ± 0.9 ^a	35.2 ± 4.3	1.1 ± 0.6 ^a	-
125	M	2.8 ± 0.7	65.3 ± 1.1	86.1 ± 15.0	2.3 ± 0.6 ^a	-
125	F	3.9 ± 1.1	64.3 ± 1.6	105.5 ± 16.0	1.6 ± 0.3 ^a	-
25	M	3.3 ± 0.7	68.9 ± 1.5	79.4 ± 12.6	3.8 ± 1.0	-
25	F	3.4 ± 0.9	65.6 ± 2.3	108.7 ± 11.6	2.9 ± 0.7	-
5	M	3.7 ± 0.6	71.4 ± 0.8	76.1 ± 13.1	5.0 ± 1.0	-
5	F	4.2 ± 1.1	70.1 ± 2.2	105.2 ± 16.6	3.0 ± 0.7	-
1	M	3.5 ± 0.6	65.0 ± 1.1	68.7 ± 9.9	4.0 ± 1.0	-
1	F	3.2 ± 0.9	63.1 ± 1.6	116.7 ± 17.6	2.5 ± 0.7	-
0	M	3.8 ± 0.5	69.3 ± 2.7	72.0 ± 21.5	4.5 ± 0.8	5.8 ± 0.4 ^{aa}
0	F	4.1 ± 1.0	65.2 ± 2.9	106.8 ± 25.0	3.3 ± 0.8	6.4 ± 0.9 ^{aa}
Amitrole						
(ppm)						
50	M	5.8 ± 3.1	71.4 ± 1.5	67.3 ± 11.8	3.6 ± 1.3	-
50	F	4.8 ± 3.2	69.6 ± 2.1	94.8 ± 13.3	3.5 ± 1.2	-
PTU						
(ppm)						
125	M	4.7 ± 1.7	59.1 ± 1.3 ^a	73.2 ± 9.9 ^a	0.6 ± 0.2 ^a	9.4 ± 1.3 ^a
125	F	5.6 ± 2.5	60.4 ± 1.7 ^a	69.6 ± 9.4 ^a	0.4 ± 0.2 ^a	10.7 ± 2.1 ^a

^a Significantly different (p < 0.05) from corresponding control.

^{aa} TSH values to be used as control for PTU group.

TABLE 6. FREE THYROID INDEX

FTU (pm)	Sex	Days on Study		
		30	60	90
625	M	0.52	0.15	0.68
625	F	0.67	0.12	0.70
125	M	1.62	1.06	1.48
125	F	1.27	1.35	1.05
25	M	3.69	2.12	2.64
25	F	2.42	1.91	1.90
5	M	3.24	3.27	3.53
5	F	2.00	1.88	2.12
1	M	3.28	3.45	2.64
1	F	2.22	1.86	1.52
0	M	3.17	3.52	3.12
0	F	2.52	2.31	2.16
Amicrol				
(pm)				
50	M	0.35	4.37	2.53
50	F	0.15	2.62	2.41
PTU				
(pm)				
125	M	0.66	0.74	0.33
125	F	0.69	0.68	0.23

TABLE 7. WEEKLY DIET CONSUMPTION*

Effi (gpm)	Sex	Week No. 1	Week No. 2	Week No. 3	Week No. 4	Week No. 5	Week No. 6
625	M	91.2 ± 14.1	114.6 ± 24.5	102.0 ± 14.8	106.7 ± 16.3	98.5 ± 17.2	101.0 ± 20.8
625	F	85.0 ± 14.9	103.8 ± 30.7	83.9 ± 24.2	84.0 ± 17.2	82.2 ± 24.1	75.2 ± 23.9
125	M	120.3 ± 27.0	141.9 ± 19.5	152.7 ± 29.6	152.6 ± 27.3	171.3 ± 35.2	159.6 ± 27.1
125	F	105.8 ± 33.5	105.7 ± 18.7	115.8 ± 22.9	126.8 ± 42.2	136.8 ± 58.3	124.5 ± 31.4
25	M	114.7 ± 27.0	153.6 ± 17.0	165.3 ± 23.6	166.6 ± 18.7	269.2 ± 13.6	172.1 ± 24.9
25	F	95.3 ± 20.8	119.8 ± 22.9	129.8 ± 37.9	127.1 ± 27.6	116.6 ± 17.5	121.1 ± 25.1
5	M	136.2 ± 18.9	155.4 ± 20.5	167.9 ± 26.8	171.2 ± 36.1	169.0 ± 21.1	174.3 ± 19.8
5	F	121.6 ± 24.8	115.4 ± 23.2	123.1 ± 19.9	129.3 ± 38.7	128.7 ± 29.3	128.8 ± 20.7
1	M	137.0 ± 18.0	143.5 ± 26.0	171.1 ± 28.1	171.9 ± 41.5	168.8 ± 13.4	179.0 ± 27.3
1	F	132.3 ± 13.6	116.5 ± 23.2	123.1 ± 27.9	121.2 ± 29.3	120.9 ± 23.3	140.3 ± 43.4
0	M	145.5 ± 35.2	151.1 ± 20.4	169.9 ± 21.5	168.0 ± 20.3	176.7 ± 35.0	182.9 ± 47.7
0	F	123.3 ± 43.3	119.1 ± 22.8	131.7 ± 43.2	131.6 ± 39.1	140.9 ± 39.7	146.3 ± 59.2
<i>Antennule</i>							
50	M	138.4 ± 16.4	146.1 ± 17.6	162.3 ± 19.8	165.6 ± 19.9	175.8 ± 26.0	189.9 ± 30.9
50	F	114.0 ± 19.2	118.8 ± 26.8	127.3 ± 31.7	133.3 ± 32.9	130.2 ± 26.9	127.1 ± 26.8
<i>Ant</i>							
125	M	150.6 ± 17.7	126.7 ± 17.5	113.6 ± 23.4	100.1 ± 17.2	106.1 ± 14.5	96.8 ± 18.7
125	F	120.7 ± 23.8	108.6 ± 16.6	95.5 ± 23.7	74.4 ± 13.3	86.7 ± 27.6	89.1 ± 21.2

TABLE 7. (Continued)

STI (gpm)	Sex	Week No. 7	Week No. 8	Week No. 9	Week No. 10	Week No. 11	Week No. 12
625	M	107.8 ± 17.9	117.9 ± 15.3	117.8 ± 20.7	121.0 ± 20.1	114.8 ± 17.2	91.6 ± 18.7
625	F	92.6 ± 24.8	105.2 ± 20.8	106.1 ± 27.1	101.8 ± 20.8	93.8 ± 13.5	89.8 ± 30.2
125	M	105.0 ± 13.7	178.2 ± 43.2	167.6 ± 38.4	176.7 ± 29.5	181.2 ± 46.8	164.3 ± 27.9
125	F	114.7 ± 11.9	120.5 ± 21.2	163.1 ± 83.1	146.8 ± 54.8	137.1 ± 50.9	129.6 ± 56.9
25	M	108.7 ± 43.9	183.5 ± 23.1	195.3 ± 34.4	176.4 ± 16.3	198.2 ± 51.7	200.7 ± 59.8
25	F	138.3 ± 32.9	139.0 ± 43.3	143.3 ± 36.9	133.0 ± 26.1	151.4 ± 63.1	170.0 ± 69.4
5	M	173.6 ± 27.7	181.0 ± 37.4	173.2 ± 31.2	158.6 ± 35.3	172.9 ± 38.3	156.2 ± 18.0
5	F	125.2 ± 26.9	133.9 ± 51.9	138.7 ± 25.4	127.6 ± 47.0	129.7 ± 24.3	111.1 ± 16.5
1	M	181.9 ± 45.9	182.9 ± 33.2	182.7 ± 27.9	207.8 ± 56.2	207.9 ± 54.2	169.8 ± 18.0
1	F	144.6 ± 53.2	131.9 ± 34.3	148.0 ± 46.7	145.8 ± 49.1	148.1 ± 61.5	169.6 ± 14.9
0	M	181.6 ± 48.7	181.8 ± 48.7	177.8 ± 30.5	186.5 ± 40.4	183.4 ± 45.0	177.8 ± 46.2
0	F	146.8 ± 48.7	146.6 ± 55.8	138.1 ± 36.2	153.7 ± 66.6	149.0 ± 66.8	131.7 ± 50.9
<i>Amelirade</i> (gpm)							
50	M	177.6 ± 40.8	182.1 ± 38.0	185.9 ± 39.9	229.1 ± 75.6	265.8 ± 22.0	192.5 ± 32.1
50	F	138.0 ± 51.6	132.9 ± 48.4	129.2 ± 40.8	174.6 ± 79.8	118.4 ± 25.7	138.1 ± 54.0
<i>PTG</i> (gpm)							
125	M	102.7 ± 19.0	98.4 ± 18.9	91.5 ± 19.4	101.9 ± 16.5	91.5 ± 18.1	92.0 ± 14.1
125	F	95.5 ± 19.5	91.3 ± 28.1	96.5 ± 28.3	89.1 ± 20.6	88.5 ± 9.9	88.2 ± 17.4

* Mean ± S.D.; presented in grams.

TABLE 8. WEEKLY TEST CHEMICAL IMGESTION*

EST	Sex	Week No. 1	Week No. 2	Week No. 3	Week No. 4	Week No. 5	Week No. 6	Week No. 7	Week No. 8	Week No. 9	Week No. 10	Week No. 11	Week No. 12
625	M	57.0	71.4	63.7	62.9	61.6	63.1	67.4	73.7	73.6	75.6	71.7	57.3
625	F	53.1	64.9	52.4	52.5	51.4	53.3	57.9	65.7	66.3	63.6	58.6	56.1
125	M	15.0	17.7	19.1	18.8	21.4	19.9	20.6	22.3	21.0	22.1	22.7	20.5
125	F	13.2	13.5	14.5	15.9	17.1	15.6	14.3	15.1	20.4	18.3	17.1	16.2
125	M	2.9	3.8	4.1	4.2	4.2	4.3	4.7	4.6	4.9	4.4	5.0	5.0
125	F	2.4	3.6	3.3	3.7	2.9	3.0	3.5	3.5	3.6	3.1	3.8	4.3
5	M	0.7	0.8	0.8	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.9	0.9
5	F	0.6	0.6	0.6	0.7	0.6	0.6	0.6	0.7	0.7	0.6	0.7	0.6
1	M	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
1	F	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.1
0	M	0	0	0	0	0	0	0	0	0	0	0	0
0	F	0	0	0	0	0	0	0	0	0	0	0	0
<i>Androsterone</i>													
50	M	6.9	7.3	8.1	8.3	8.8	8.5	8.9	9.1	9.3	11.5	8.3	9.6
50	F	5.7	5.9	6.4	6.7	6.5	6.4	6.9	6.7	6.5	8.7	5.9	6.9
<i>PTD</i>													
125	M	18.8	17.1	18.2	22.5	12.0	12.1	12.8	12.1	11.4	12.7	11.4	11.5
125	F	15.1	13.6	11.9	9.3	10.8	11.1	11.9	11.4	12.1	11.1	8.6	11.0

* Mean, $\pm$ S. D.; presented in grams.

TABLE 9. *Continued*

Enl. type	Sex	Weeks on Study						
		0	1	2	3	4	5	6
625	M	129.4 ± 14.2	142.4 ± 15.0	157.7 ± 17.8	172.1 ± 24.3	187.2 ± 25.3	195.1 ± 21.1	189.6 ± 26.5
	F	117.5 ± 12.0	127.2 ± 12.6	135.5 ± 12.6	143.6 ± 15.8	148.6 ± 17.5	152.6 ± 16.2	145.7 ± 21.5
125	M	132.1 ± 17.5	150.3 ± 22.7	226.7 ± 24.6	274.0 ± 27.8	306.6 ± 37.3	341.3 ± 39.2	365.7 ± 38.0
	F	116.6 ± 14.6	146.3 ± 13.1	168.2 ± 15.1	188.9 ± 16.0	204.1 ± 20.8	217.3 ± 25.6	230.7 ± 23.0
25	M	145.2 ± 11.3	189.6 ± 18.1	242.1 ± 15.2	295.0 ± 20.0	335.9 ± 21.9	376.9 ± 22.9	401.3 ± 21.3
	F	127.2 ± 12.1	152.1 ± 13.3	176.5 ± 14.6	198.7 ± 16.6	217.4 ± 18.4	229.8 ± 20.6	241.0 ± 23.8
5	M	140.5 ± 13.9	195.3 ± 14.4	248.9 ± 21.5	299.8 ± 22.9	340.1 ± 28.8	373.9 ± 30.6	348.5 ± 36.3
	F	126.0 ± 12.4	155.1 ± 11.4	179.4 ± 23.9	201.6 ± 19.6	218.2 ± 21.5	238.5 ± 22.8	254.1 ± 22.0
1	M	130.0 ± 16.6	191.5 ± 22.1	254.0 ± 29.9	292.7 ± 32.7	332.3 ± 35.2	377.5 ± 37.6	408.6 ± 46.9
	F	115.2 ± 13.7	151.6 ± 13.9	173.4 ± 14.7	193.6 ± 17.3	213.3 ± 20.2	227.4 ± 17.8	238.1 ± 18.4
0	M	141.0 ± 27.9	193.8 ± 29.4	262.9 ± 30.1	240.5 ± 34.9	331.9 ± 35.8	346.4 ± 35.3	394.5 ± 33.6
	F	119.0 ± 21.1	151.6 ± 18.0	176.0 ± 22.2	194.5 ± 21.5	211.0 ± 20.1	228.9 ± 21.6	242.3 ± 23.7
Amniotic	M	137.1 ± 18.7	149.5 ± 20.8	245.3 ± 25.7	291.5 ± 27.5	329.6 ± 27.2	361.6 ± 33.5	379.3 ± 37.5
	F	120.2 ± 13.7	155.5 ± 16.2	176.7 ± 19.0	195.1 ± 23.7	216.5 ± 21.6	232.6 ± 24.8	243.4 ± 23.9
PTU	M	168.5 ± 30.6	224.3 ± 35.2	243.9 ± 37.0	245.3 ± 34.9	267.4 ± 32.1	281.7 ± 30.2	295.0 ± 29.3
	F	136.4 ± 26.6	167.8 ± 22.5	174.1 ± 24.3	176.3 ± 25.8	179.1 ± 28.2	183.5 ± 26.9	185.0 ± 26.7

TABLE 9. (Continued)

Weeks on Study	Sex	Weeks on Study									
		7	8	9	10	11	12				
625	M	195.7 ± 36.0	210.7 ± 34.6	234.8 ± 29.8	246.6 ± 34.8	251.2 ± 30.2	239.4 ± 40.3				
625	F	148.8 ± 25.0	161.9 ± 21.6	170.3 ± 25.7	180.7 ± 23.1	181.3 ± 23.9	171.5 ± 28.3				
125	M	385.3 ± 40.5	413.4 ± 32.3	431.4 ± 36.7	444.6 ± 40.2	462.5 ± 40.9	472.1 ± 43.3				
125	F	242.1 ± 23.4	249.9 ± 26.6	250.8 ± 22.6	254.5 ± 25.5	265.7 ± 26.4	268.1 ± 23.4				
25	M	420.1 ± 29.0	443.0 ± 26.0	451.9 ± 29.2	466.4 ± 26.2	483.5 ± 33.1	497.5 ± 33.8				
25	F	250.9 ± 22.9	254.3 ± 25.6	273.6 ± 25.0	275.2 ± 23.1	283.3 ± 23.3	288.8 ± 26.9				
5	M	425.1 ± 39.4	447.8 ± 42.2	457.7 ± 38.4	468.7 ± 35.4	478.8 ± 38.5	491.9 ± 39.2				
5	F	243.3 ± 24.1	269.6 ± 25.4	270.9 ± 26.5	286.7 ± 25.8	290.2 ± 23.4	295.2 ± 26.8				
1	M	428.6 ± 44.4	446.7 ± 49.7	442.0 ± 49.0	462.0 ± 49.4	476.0 ± 52.9	492.3 ± 55.3				
1	F	249.1 ± 19.6	256.5 ± 19.1	260.0 ± 20.8	267.5 ± 20.1	269.8 ± 24.0	276.3 ± 22.2				
0	M	417.9 ± 36.0	437.9 ± 39.7	440.9 ± 35.7	462.1 ± 38.8	478.4 ± 33.7	492.1 ± 35.2				
0	F	251.1 ± 22.0	263.3 ± 30.6	266.6 ± 30.5	275.2 ± 26.6	280.5 ± 28.0	285.9 ± 30.7				
Seminarole											
50	M	407.4 ± 37.0	428.8 ± 44.2	437.5 ± 44.4	456.4 ± 40.1	471.1 ± 40.0	487.7 ± 40.4				
50	F	249.8 ± 22.7	258.2 ± 25.8	254.9 ± 32.8	263.8 ± 31.2	262.0 ± 32.2	275.5 ± 32.6				
PMS											
125	M	265.5 ± 30.4	285.7 ± 31.0	259.0 ± 33.0	259.3 ± 35.5	265.3 ± 35.7	265.6 ± 37.2				
125	F	184.9 ± 27.5	183.7 ± 27.8	171.8 ± 28.0	171.2 ± 28.9	172.4 ± 27.6	174.5 ± 29.0				

* Mean, ± S.D., presented in grams.

1	1	4	9	16	25	36	49	64	81	100	121	144	169	196	225	256	289	324	361	400	441	484	529	576	625	676	729	784	841	900	961	1024	1089	1156	1225	1296	1369	1444	1521	1600	1681	1764	1849	1936	2025	2116	2209	2304	2401	2500	2601	2704	2809	2916	3025	3136	3249	3364	3481	3600	3721	3844	3969	4096	4225	4356	4489	4624	4761	4900	5041	5184	5329	5476	5625	5776	5929	6084	6241	6400	6561	6724	6889	7056	7225	7396	7569	7744	7921	8100	8281	8464	8649	8836	9025	9216	9409	9604	9801	10000																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										
2	4	16	36	64	100	144	196	256	324	400	484	576	676	784	900	1024	1156	1296	1444	1600	1764	1936	2116	2304	2500	2704	2916	3136	3364	3600	3844	4096	4356	4624	4900	5184	5476	5776	6084	6400	6724	7056	7396	7744	8100	8464	8836	9216	9604	10000	10404	10816	11236	11664	12100	12544	13000	13464	13936	14416	14904	15400	15904	16416	16936	17464	18000	18544	19096	19656	20224	20800	21384	21976	22576	23184	23800	24424	25056	25696	26344	26996	27656	28324	29000	29684	30376	31076	31784	32500	33224	33956	34696	35444	36200	36964	37736	38516	39304	40100	40904	41716	42536	43364	44200	45044	45896	46756	47624	48500	49384	50276	51176	52084	52996	53916	54844	55780	56724	57676	58636	59604	60580	61564	62556	63556	64564	65580	66604	67636	68676	69724	70780	71844	72916	73996	75084	76180	77284	78396	79516	80644	81780	82924	84076	85236	86404	87580	88764	89956	91156	92364	93580	94804	96036	97276	98524	99780	101044	102316	103596	104884	106180	107484	108796	110116	111444	112780	114124	115476	116836	118204	119580	120964	122356	123756	125164	126580	127996	129420	130852	132292	133740	135196	136660	138132	139612	141096	142596	144104	145620	147144	148676	150216	151764	153320	154884	156456	158036	159624	161220	162824	164436	166056	167684	169320	170964	172616	174276	175944	177620	179304	180996	182696	184404	186120	187844	189576	191316	193064	194820	196584	198356	200136	201924	203720	205524	207336	209156	210984	212820	214664	216516	218376	220244	222120	224004	225896	227796	229704	231620	233544	235476	237416	239364	241320	243284	245256	247236	249224	251220	253224	255236	257256	259284	261320	263364	265416	267476	269544	271620	273704	275796	277896	279996	282096	284196	286296	288396	290496	292596	294696	296796	298896	300996	303096	305196	307296	309396	311496	313596	315696	317796	319896	321996	324096	326196	328296	330396	332496	334596	336696	338796	340896	342996	345096	347196	349296	351396	353496	355596	357696	359796	361896	363996	366096	368196	370296	372396	374496	376596	378696	380796	382896	384996	387096	389196	391296	393396	395496	397596	399696	401796	403896	405996	408096	410196	412296	414396	416496	418596	420696	422796	424896	426996	429096	431196	433296	435396	437496	439596	441696	443796	445896	447996	450096	452196	454296	456396	458496	460596	462696	464796	466896	468996	471096	473196	475296	477396	479496	481596	483696	485796	487896	489996	492096	494196	496296	498396	500496	502596	504696	506796	508896	510996	513096	515196	517296	519396	521496	523596	525696	527796	529896	531996	534096	536196	538296	540396	542496	544596	546696	548796	550896	552996	555096	557196	559296	561396	563496	565596	567696	569796	571896	573996	576096	578196	580296	582396	584496	586596	588696	590796	592896	594996	597096	599196	601296	603396	605496	607596	609696	611796	613896	615996	618096	620196	622296	624396	626496	628596	630696	632796	634896	636996	639096	641196	643296	645396	647496	649596	651696	653796	655896	657996	660096	662196	664296	666396	668496	670596	672696	674796	676896	678996	681096	683196	685296	687396	689496	691596	693696	695796	697896	699996	702096	704196	706296	708396	710496	712596	714696	716796	718896	720996	723096	725196	727296	729396	731496	733596	735696	737796	739896	741996	744096	746196	748296	750396	752496	754596	756696	758796	760896	762996	765096	767196	769296	771396	773496	775596	777696	779796	781896	783996	786096	788196	790296	792396	794496	796596	798696	800796	802896	804996	807096	809196	811296	813396	815496	817596	819696	821796	823896	825996	828096	830196	832296	834396	836496	838596	840696	842796	844896	846996	849096	851196	853296	855396	857496	859596	861696	863796	865896	867996	870096	872196	874296	876396	878496	880596	882696	884796	886896	888996	891096	893196	895296	897396	899496	901596	903696	905796	907896	909996	912096	914196	916296	918396	920496	922596	924696	926796	928896	930996	933096	935196	937296	939396	941496	943596	945696	947796	949896	951996	954096	956196	958296	960396	962496	964596	966696	968796	970896	972996	975096	977196	979296	981396	983496	985596	987696	989796	991896	993996	996096	998196	1000296	1002396	1004496	1006596	1008696	1010796	1012896	1014996	1017096	1019196	1021296	1023396	1025496	1027596	1029696	1031796	1033896	1035996	1038096	1040196	1042296	1044396	1046496	1048596	1050696	1052796	1054896	1056996	1059096	1061196	1063296	1065396	1067496	1069596	1071696	1073796	1075896	1077996	1080096	1082196	1084296	1086396	1088496	1090596	1092696	1094796	1096896	1098996	1101096	1103196	1105296	1107396	1109496	1111596	1113696	1115796	1117896	1119996	1122096	1124196	1126296	1128396	1130496	1132596	1134696	1136796	1138896	1140996	1143096	1145196	1147296	1149396	1151496	1153596	1155696	1157796	1159896	1161996	1164096	1166196	1168296	1170396	1172496	1174596	1176696	1178796	1180896	1182996	1185096	1187196	1189296	1191396	1193496	1195596	1197696	1199796	1201896	1203996	1206096	1208196	1210296	1212396	1214496	1216596	1218696	1220796	1222896	1224996	1227096	1229196	1231296	1233396	1235496	1237596	1239696	1241796	1243896	1245996	1248096	1250196	1252296	1254396	1256496	1258596	1260696	1262796	1264896	1266996	1269096	1271196	1273296	1275396	1277496	1279596	1281696	1283796	1285896	1287996	1290096	1292196	1294296	1296396	1298496	1300596	1302696	1304796	1306896	1308996	1311096	1313196	1315296	1317396	1319496	1321596	1323696	1325796	1327896	1329996	1332096	1334196	1336296	1338396	1340496	1342596	1344696	1346796	1348896	1350996	1353096	1355196	1357296	1359396	1361496	1363596	1365696	1367796	1369896	1371996	1374096	1376196	1378296	1380396	1382496	1384596	1386696	1388796	1390896	1392996	1395096	1397196	1399296	1401396	1403496	1405596	1407696	1409796	1411896	1413996	1416096	1418196	1420296	1422396	1424496	1426596	1428696	1430796	1432896	1434996	1437096	1439196	1441296	1443396	1445496	1447596	1449696	1451796	1453896	1455996	1458096	1460196	1462296	1464396	1466496	1468596	1470696	1472796	1474896	1476996	1479096	1481196	1483296	1485396	1487496	1489596	1491696	1493796	1495896	1497996	1499996	1502096	1504196	1506296	1508396	1510496	1512596	1514696	1516796	1518896	1520996	1523096	1525196	1527296	1529396	1531496	1533596	1535696	1537796	1539896	1541996	1544096	1546196	1548296	1550396	1552496	1554596	1556696	1558796	1560896	1562996	1565096	1567196	1569296	1571396	1573496	1575596	1577696	1579796	1581896	1583996	1586096	1588196	1590296	1592396	1594496	1596596	1598696	1600796	1602896	1604996	1607096	1609196	1611296	1613396	1615496	1617596	1619696	1621796	1623896	1625996	1628096	1630196	1632296	1634396	1636496	1638596	1640696	1642796	1644896	1646996	1649096	1651196	1653296	1655396	1657496	1659596	1661696	1663796	1665896	1667996	1670096	1672196	1674296	1676396	1678496	1680596	1682696	1684796	1686896	1688996	1691096	1693196	1695296	1697396	1699496	1701596	1703696	1705796	1707896	1709996	1712096	1714196	1716296	1718396	1720496	1722596	1724696	1726796	1728896	1730996	1733096	1735196	1737296	1739396	1741496	1743596	1745696	1747796	1749896	1751996	1754096	1756196	1758296	1760396	1762496	1764596	1766696	1768796	1770896	1772996	1775096	1777196	1779296	1781396	1783496	1785596	1787696	1789796	1791896	1793996	1796096	1798196	1800296	1802396	1804496	1806596	1808696	1810796	1812896	1814996	1817096	1819196	1821296	1823396	1825496	1827596	1829696	1831796	1833896	1835996	1838096	1840196	1842296	1844396	1846496	1848596	1850696	1852796	1854896	1856996	1859096	1861196	1863296	1865396	1867496	18695

1. *Journal of Management Education*, 2000, 24(1), 10-19.

Year	Age	Sex	Height (in)	Weight (lb)	Arm span (in)	Forearm (in)	Hand (in)	Thumb (in)	Index (in)	Middle (in)	Ring (in)	Pinky (in)	Width (in)	Depth (in)	Volume (cc)	Area (sq in)	Perimeter (in)	Volume (cc)	Area (sq in)	Perimeter (in)
1900	10	M	58	110	68	22	10	6	8	10	12	14	16	18	20	22	24	26	28	30
1901	11	M	60	120	70	23	11	7	9	11	13	15	17	19	21	23	25	27	29	31
1902	12	M	62	130	72	24	12	8	10	12	14	16	18	20	22	24	26	28	30	32
1903	13	M	64	140	74	25	13	9	11	13	15	17	19	21	23	25	27	29	31	33
1904	14	M	66	150	76	26	14	10	12	14	16	18	20	22	24	26	28	30	32	34
1905	15	M	68	160	78	27	15	11	13	15	17	19	21	23	25	27	29	31	33	35
1906	16	M	70	170	80	28	16	12	14	16	18	20	22	24	26	28	30	32	34	36
1907	17	M	72	180	82	29	17	13	15	17	19	21	23	25	27	29	31	33	35	37
1908	18	M	74	190	84	30	18	14	16	18	20	22	24	26	28	30	32	34	36	38
1909	19	M	76	200	86	31	19	15	17	19	21	23	25	27	29	31	33	35	37	39
1910	20	M	78	210	88	32	20	16	18	20	22	24	26	28	30	32	34	36	38	40
1911	21	M	80	220	90	33	21	17	19	21	23	25	27	29	31	33	35	37	39	41
1912	22	M	82	230	92	34	22	18	20	22	24	26	28	30	32	34	36	38	40	42
1913	23	M	84	240	94	35	23	19	21	23	25	27	29	31	33	35	37	39	41	43
1914	24	M	86	250	96	36	24	20	22	24	26	28	30	32	34	36	38	40	42	44
1915	25	M	88	260	98	37	25	21	23	25	27	29	31	33	35	37	39	41	43	45
1916	26	M	90	270	100	38	26	22	24	26	28	30	32	34	36	38	40	42	44	46
1917	27	M	92	280	102	39	27	23	25	27	29	31	33	35	37	39	41	43	45	47
1918	28	M	94	290	104	40	28	24	26	28	30	32	34	36	38	40	42	44	46	48
1919	29	M	96	300	106	41	29	25	27	29	31	33	35	37	39	41	43	45	47	49
1920	30	M	98	310	108	42	30	26	28	30	32	34	36	38	40	42	44	46	48	50
1921	31	M	100	320	110	43	31	27	29	31	33	35	37	39	41	43	45	47	49	51
1922	32	M	102	330	112	44	32	28	30	32	34	36	38	40	42	44	46	48	50	52
1923	33	M	104	340	114	45	33	29	31	33	35	37	39	41	43	45	47	49	51	53
1924	34	M	106	350	116	46	34	30	32	34	36	38	40	42	44	46	48	50	52	54
1925	35	M	108	360	118	47	35	31	33	35	37	39	41	43	45	47	49	51	53	55
1926	36	M	110	370	120	48	36	32	34	36	38	40	42	44	46	48	50	52	54	56
1927	37	M	112	380	122	49	37	33	35	37	39	41	43	45	47	49	51	53	55	57
1928	38	M	114	390	124	50	38	34	36	38	40	42	44	46	48	50	52	54	56	58
1929	39	M	116	400	126	51	39	35	37	39	41	43	45	47	49	51	53	55	57	59
1930	40	M	118	410	128	52	40	36	38	40	42	44	46	48	50	52	54	56	58	60
1931	41	M	120	420	130	53	41	37	39	41	43	45	47	49	51	53	55	57	59	61
1932	42	M	122	430	132	54	42	38	40	42	44	46	48	50	52	54	56	58	60	62
1933	43	M	124	440	134	55	43	39	41	43	45	47	49	51	53	55	57	59	61	63
1934	44	M	126	450	136	56	44	40	42	44	46	48	50	52	54	56	58	60	62	64
1935	45	M	128	460	138	57	45	41	43	45	47	49	51	53	55	57	59	61	63	65
1936	46	M	130	470	140	58	46	42	44	46	48	50	52	54	56	58	60	62	64	66
1937	47	M	132	480	142	59	47	43	45	47	49	51	53	55	57	59	61	63	65	67
1938	48	M	134	490	144	60	48	44	46	48	50	52	54	56	58	60	62	64	66	68
1939	49	M	136	500	146	61	49	45	47	49	51	53	55	57	59	61	63	65	67	69
1940	50	M	138	510	148	62	50	46	48	50	52	54	56	58	60	62	64	66	68	70
1941	51	M	140	520	150	63	51	47	49	51	53	55	57	59	61	63	65	67	69	71
1942	52	M	142	530	152	64	52	48	50	52	54	56	58	60	62	64	66	68	70	72
1943	53	M	144	540	154	65	53	49	51	53	55	57	59	61	63	65	67	69	71	73
1944	54	M	146	550	156	66	54	50	52	54	56	58	60	62	64	66	68	70	72	74
1945	55	M	148	560	158	67	55	51	53	55	57	59	61	63	65	67	69	71	73	75
1946	56	M	150	570	160	68	56	52	54	56	58	60	62	64	66	68	70	72	74	76
1947	57	M	152	580	162	69	57	53	55	57	59	61	63	65	67	69	71	73	75	77
1948	58	M	154	590	164	70	58	54	56	58	60	62	64	66	68	70	72	74	76	78
1949	59	M	156	600	166	71	59	55	57	59	61	63	65	67	69	71	73	75	77	79
1950	60	M	158	610	168	72	60	56	58	60	62	64	66	68	70	72	74	76	78	80
1951	61	M	160	620	170	73	61	57	59	61	63	65	67	69	71	73	75	77	79	81
1952	62	M	162	630	172	74	62	58	60	62	64	66	68	70	72	74	76	78	80	82
1953	63	M	164	640	174	75	63	59	61	63	65	67	69	71	73	75	77	79	81	83
1954	64	M	166	650	176	76	64	60	62	64	66	68	70	72	74	76	78	80	82	84
1955	65	M	168	660	178	77	65	61	63	65	67	69	71	73	75	77	79	81	83	85
1956	66	M	170	670	180	78	66	62	64	66	68	70	72	74	76	78	80	82	84	86
1957	67	M	172	680	182	79	67	63	65	67	69	71	73	75	77	79	81	83	85	87
1958	68	M	174	690	184	80	68	64	66	68	70	72	74	76	78	80	82	84	86	88
1959	69	M	176	700	186	81	69	65	67	69	71	73	75	77	79	81	83	85	87	89
1960	70	M	178	710	188	82	70	66	68	70	72	74	76	78	80	82	84	86	88	90
1961	71	M	180	720	190	83	71	67	69	71	73	75	77	79	81	83	85	87	89	91
1962	72	M	182	730	192	84	72	68	70	72	74	76	78	80	82	84	86	88	90	92
1963	73	M	184	740	194	85	73	69	71	73	75	77	79	81	83	85	87	89	91	93
1964	74	M	186	750	196	86	74	70	72	74	76	78	80	82	84	86	88	90	92	94
1965	75	M	188	760	198	87	75	71	73	75	77	79	81	83	85	87	89	91	93	95
1966	76	M	190	770	200	88	76	72	74	76	78	80	82	84	86	88	90	92	94	96
1967	77	M	192	780	202	89	77	73	75	77	79	81	83	85	87	89	91	93	95	97
1968	78	M	194	790	204	90	78	74	76	78	80	82	84	86	88	90	92	94	96	98
1969	79	M	196	800	206	91	79	75	77	79	81	83	85	87	89	91	93	95	97	99
1970	80	M	198	810	208	92	80	76	78	80	82	84	86	88	90	92	94	96	98	100
1971	81	M	200	820	210	93	81	77	79	81	83	85	87	89	91	93	95	97	99	101
1972	82	M	202	830	212	94	82	78	80	82	84	86	88	90	92	94	96	98	100	102
1973	83	M	204	840	214	95	83	79	81	83	85	87	89	91	93	95	97	99	101	103
1974	84	M	206	850	216	96	84	80	82	84	86	88	90	92	94	96	98	100	102	104
1975	85	M	208	860	218	97	85	81	83	85	87	89	91	93	95	97	99	101	103	105
1976	86	M	210	870	220	98	86	82	84	86	88	90	92	94	96	98	100	102	104	106
1977	87	M	212	880	222	99	87	83	85	87	89	91	93	95	97	99	101	103	105	107
1978	88	M	214	890	224	100	88	84	86	88	90	92	94	96	98	100	102	104	106	108
1979	89	M	216	900	226	101	89													

TABLE 11. ORGAN WEIGHT:BODY WEIGHT RATIO

ETU (ppm)	Days on Study	Sex	Heart (g)	Spleen (g)	Rt. Kidney (g)	Ovary (paired, g)	Testicle (paired, g)
625	90	M	3.63×10^{-3}	1.35×10^{-3}	3.99×10^{-3}	--	2.07×10^{-2}
625	90	F	3.44×10^{-3}	1.41×10^{-3}	3.81×10^{-3}	4.60×10^{-4}	--
125	90	M	2.82×10^{-3}	1.70×10^{-3}	3.41×10^{-3}	--	1.06×10^{-2}
125	90	F	3.25×10^{-3}	1.93×10^{-3}	3.41×10^{-3}	3.43×10^{-4}	--
25	90	M	2.78×10^{-3}	1.66×10^{-3}	3.13×10^{-3}	--	1.05×10^{-2}
25	90	F	3.29×10^{-3}	1.79×10^{-3}	3.42×10^{-3}	3.31×10^{-4}	--
5	90	M	2.85×10^{-3}	1.78×10^{-3}	3.01×10^{-3}	--	1.07×10^{-2}
5	90	F	3.13×10^{-3}	1.83×10^{-3}	3.48×10^{-3}	3.71×10^{-4}	--
1	90	M	2.73×10^{-3}	1.56×10^{-3}	3.04×10^{-3}	--	1.01×10^{-2}
1	90	F	2.99×10^{-3}	1.84×10^{-3}	3.34×10^{-3}	3.70×10^{-4}	--
0	90	M	2.72×10^{-3}	1.71×10^{-3}	3.09×10^{-3}	--	1.08×10^{-2}
0	90	F	3.28×10^{-3}	1.95×10^{-3}	3.56×10^{-3}	3.56×10^{-4}	--
625	60	M	3.79×10^{-3}	1.53×10^{-3}	4.26×10^{-3}	--	2.06×10^{-2}
625	60	F	3.68×10^{-3}	1.35×10^{-3}	4.34×10^{-3}	5.25×10^{-4}	--
125	60	M	3.20×10^{-3}	1.81×10^{-3}	3.51×10^{-3}	--	1.10×10^{-2}
125	60	F	3.76×10^{-3}	2.13×10^{-3}	3.75×10^{-3}	5.21×10^{-4}	--
25	60	M	2.94×10^{-3}	1.70×10^{-3}	3.50×10^{-3}	--	1.14×10^{-2}
25	60	F	3.46×10^{-3}	2.09×10^{-3}	3.92×10^{-3}	3.80×10^{-4}	--
5	60	M	3.05×10^{-3}	1.79×10^{-3}	3.51×10^{-3}	--	1.88×10^{-2}
5	60	F	3.43×10^{-3}	2.02×10^{-3}	3.57×10^{-3}	3.85×10^{-4}	--
1	60	M	2.78×10^{-3}	1.56×10^{-3}	3.37×10^{-3}	--	1.09×10^{-2}
1	60	F	3.19×10^{-3}	2.12×10^{-3}	3.78×10^{-3}	3.99×10^{-4}	--
0	60	M	2.97×10^{-3}	1.63×10^{-3}	3.60×10^{-3}	--	1.08×10^{-2}
0	60	F	3.33×10^{-3}	2.07×10^{-3}	3.87×10^{-3}	4.40×10^{-4}	--
625	30	M	3.28×10^{-3}	1.80×10^{-3}	4.29×10^{-3}	--	2.06×10^{-2}
625	30	F	3.39×10^{-3}	1.81×10^{-3}	4.21×10^{-3}	5.79×10^{-4}	--
125	30	M	3.25×10^{-3}	2.08×10^{-3}	3.89×10^{-3}	--	1.26×10^{-2}
125	30	F	3.87×10^{-3}	2.39×10^{-3}	4.20×10^{-3}	5.44×10^{-4}	--
25	30	M	3.43×10^{-3}	2.35×10^{-3}	3.86×10^{-3}	--	1.26×10^{-2}
25	30	F	3.72×10^{-3}	2.44×10^{-3}	4.16×10^{-3}	5.33×10^{-4}	--
5	30	M	3.18×10^{-3}	2.27×10^{-3}	3.82×10^{-3}	--	1.24×10^{-2}
5	30	F	3.71×10^{-3}	2.51×10^{-3}	3.97×10^{-3}	5.38×10^{-4}	--
1	30	M	3.58×10^{-3}	2.26×10^{-3}	3.89×10^{-3}	--	1.23×10^{-2}
1	30	F	3.52×10^{-3}	2.41×10^{-3}	3.85×10^{-3}	5.82×10^{-4}	--
0	30	M	3.39×10^{-3}	2.12×10^{-3}	3.86×10^{-3}	--	1.17×10^{-2}
0	30	F	3.86×10^{-3}	2.38×10^{-3}	3.77×10^{-3}	5.40×10^{-4}	--

TABLE II. (Continued)

DTU (ppm)	Days on study	Sex	Liver (g)	Pituitary (g)	Thyroid (paired, g)	Adrenal (mg)	Brain (g)
625	90	M	3.39×10^{-2}	4.79×10^{-5}	22.91×10^{-5}	1.93×10^{-4}	8.33×10^{-3}
625	90	F	3.66×10^{-2}	7.62×10^{-5}	27.10×10^{-5}	2.36×10^{-4}	9.79×10^{-3}
125	90	M	3.91×10^{-2}	2.22×10^{-5}	7.66×10^{-5}	0.99×10^{-4}	4.21×10^{-3}
125	90	F	3.39×10^{-2}	4.71×10^{-5}	6.73×10^{-5}	1.92×10^{-4}	6.66×10^{-3}
25	90	M	3.46×10^{-2}	2.06×10^{-5}	3.80×10^{-5}	1.01×10^{-4}	4.06×10^{-3}
25	90	F	3.72×10^{-2}	5.01×10^{-5}	6.88×10^{-5}	2.03×10^{-4}	6.49×10^{-3}
5	90	M	3.37×10^{-2}	2.23×10^{-5}	5.21×10^{-5}	0.99×10^{-4}	4.16×10^{-3}
5	90	F	3.72×10^{-2}	4.92×10^{-5}	6.43×10^{-5}	2.20×10^{-4}	6.34×10^{-3}
1	90	M	3.56×10^{-2}	1.93×10^{-5}	5.41×10^{-5}	0.98×10^{-4}	4.02×10^{-3}
1	90	F	3.76×10^{-2}	4.94×10^{-5}	7.14×10^{-5}	2.29×10^{-4}	6.41×10^{-3}
0	90	M	3.31×10^{-2}	2.18×10^{-5}	5.80×10^{-5}	0.98×10^{-4}	3.96×10^{-3}
0	90	F	3.60×10^{-2}	5.23×10^{-5}	8.81×10^{-5}	2.33×10^{-4}	6.46×10^{-3}
625	60	M	3.91×10^{-2}	3.03×10^{-5}	5.73×10^{-5}	2.04×10^{-4}	8.66×10^{-3}
625	60	F	4.91×10^{-2}	5.90×10^{-5}	5.90×10^{-5}	2.66×10^{-4}	10.70×10^{-3}
125	60	M	4.17×10^{-2}	3.28×10^{-5}	3.28×10^{-5}	1.34×10^{-4}	4.78×10^{-3}
125	60	F	4.03×10^{-2}	4.81×10^{-5}	4.81×10^{-5}	2.51×10^{-4}	7.35×10^{-3}
25	60	M	4.44×10^{-2}	2.22×10^{-5}	2.22×10^{-5}	1.03×10^{-4}	4.35×10^{-3}
25	60	F	4.05×10^{-2}	3.45×10^{-5}	3.45×10^{-5}	2.33×10^{-4}	7.36×10^{-3}
5	60	M	3.80×10^{-2}	1.84×10^{-5}	1.84×10^{-5}	1.02×10^{-4}	4.16×10^{-3}
5	60	F	3.93×10^{-2}	4.18×10^{-5}	4.18×10^{-5}	2.37×10^{-4}	7.03×10^{-3}
1	60	M	3.63×10^{-2}	2.00×10^{-5}	2.00×10^{-5}	1.09×10^{-4}	4.32×10^{-3}
1	60	F	3.66×10^{-2}	4.75×10^{-5}	4.75×10^{-5}	2.19×10^{-4}	7.06×10^{-3}
0	60	M	3.79×10^{-2}	2.22×10^{-5}	2.22×10^{-5}	1.13×10^{-4}	4.56×10^{-3}
0	60	F	3.82×10^{-2}	6.19×10^{-5}	4.19×10^{-5}	2.60×10^{-4}	7.06×10^{-3}
625	30	M	4.50×10^{-2}	6.82×10^{-5}	15.82×10^{-5}	2.05×10^{-4}	9.19×10^{-3}
625	30	F	5.21×10^{-2}	4.80×10^{-5}	18.90×10^{-5}	2.45×10^{-4}	11.10×10^{-3}
125	30	M	4.86×10^{-2}	3.20×10^{-5}	10.20×10^{-5}	1.60×10^{-4}	5.79×10^{-3}
125	30	F	4.43×10^{-2}	4.97×10^{-5}	11.20×10^{-5}	2.73×10^{-4}	6.54×10^{-3}
25	30	M	4.62×10^{-2}	2.38×10^{-5}	7.72×10^{-5}	1.44×10^{-4}	5.59×10^{-3}
25	30	F	4.60×10^{-2}	3.79×10^{-5}	9.89×10^{-5}	2.70×10^{-4}	8.09×10^{-3}
5	30	M	4.62×10^{-2}	2.35×10^{-5}	5.77×10^{-5}	1.43×10^{-4}	5.65×10^{-3}
5	30	F	4.24×10^{-2}	3.94×10^{-5}	7.93×10^{-5}	2.67×10^{-4}	8.46×10^{-3}
1	30	M	4.60×10^{-2}	2.39×10^{-5}	6.02×10^{-5}	1.50×10^{-4}	5.96×10^{-3}
1	30	F	4.02×10^{-2}	3.67×10^{-5}	7.06×10^{-5}	2.92×10^{-4}	8.53×10^{-3}
0	30	M	4.22×10^{-2}	5.65×10^{-5}	6.20×10^{-5}	1.26×10^{-4}	5.30×10^{-3}
0	30	F	4.43×10^{-2}	5.13×10^{-5}	7.14×10^{-5}	2.58×10^{-4}	8.11×10^{-3}

TABLE 11. (Continued)

Amitrole (ppm)	Days on Study	Sex	Heart (g)	Spleen (g)	Right Kidney (g)	Ovary (paired) (g)	Testicle (paired) (g)
50	90	M	2.66×10^{-3}	1.65×10^{-3}	3.08×10^{-3}	-	1.07×10^{-2}
50	90	F	3.04×10^{-3}	2.08×10^{-3}	3.47×10^{-3}	3.47×10^{-4}	-
50	60	M	2.83×10^{-3}	1.67×10^{-3}	3.52×10^{-3}	-	1.12×10^{-2}
50	60	F	3.45×10^{-3}	2.13×10^{-3}	3.77×10^{-3}	3.86×10^{-4}	-
50	30	M	2.83×10^{-3}	1.74×10^{-3}	3.59×10^{-3}	-	1.31×10^{-2}
50	30	F	3.32×10^{-3}	2.48×10^{-3}	3.71×10^{-3}	6.20×10^{-4}	-
PTU							
(ppm)							
125	90	M	2.66×10^{-3}	0.93×10^{-3}	2.89×10^{-3}	-	1.69×10^{-2}
125	90	F	2.82×10^{-3}	1.03×10^{-3}	3.16×10^{-3}	3.08×10^{-4}	-
125	60	M	2.58×10^{-3}	1.24×10^{-3}	3.30×10^{-3}	-	1.71×10^{-2}
125	60	F	3.03×10^{-3}	1.40×10^{-3}	3.38×10^{-3}	4.48×10^{-4}	-
125	30	M	2.76×10^{-3}	1.43×10^{-3}	3.58×10^{-3}	-	1.77×10^{-2}
125	30	F	3.10×10^{-3}	1.63×10^{-3}	3.60×10^{-3}	5.49×10^{-4}	-
Control							
0	90	M	2.72×10^{-3}	1.71×10^{-3}	3.09×10^{-3}	-	1.08×10^{-2}
0	90	F	3.26×10^{-3}	1.95×10^{-3}	3.56×10^{-3}	3.56×10^{-4}	-
0	60	M	2.58×10^{-3}	1.24×10^{-3}	3.30×10^{-3}	-	1.71×10^{-2}
0	60	F	3.03×10^{-3}	1.40×10^{-3}	3.38×10^{-3}	4.48×10^{-4}	-
0	30	M	3.39×10^{-3}	2.12×10^{-3}	3.84×10^{-3}	-	1.31×10^{-2}
0	30	F	3.84×10^{-3}	2.38×10^{-3}	3.77×10^{-3}	6.20×10^{-4}	-

TABLE 11. (Continue)

Amitrole (ppm)	Days on Study	Sex	Liver (g)	Pituitary (g)	Thyroid (paired) (g)	Adrenal (mg)
50	90	M	3.56×10^{-2}	2.56×10^{-5}	13.43×10^{-5}	0.99×10^{-4}
50	90	F	3.59×10^{-2}	5.92×10^{-5}	14.23×10^{-5}	2.09×10^{-4}
50	60	M	3.88×10^{-2}	2.33×10^{-5}	8.12×10^{-5}	1.00×10^{-4}
50	60	F	3.95×10^{-2}	5.48×10^{-5}	9.11×10^{-5}	2.52×10^{-4}
50	30	M	4.38×10^{-2}	2.69×10^{-5}	22.91×10^{-5}	1.16×10^{-3}
50	30	F	4.95×10^{-2}	3.52×10^{-5}	22.80×10^{-5}	2.44×10^{-3}
ETU (ppm)						
125	90	M	3.17×10^{-2}	3.02×10^{-5}	42.90×10^{-5}	1.08×10^{-4}
125	90	F	3.42×10^{-2}	5.19×10^{-5}	45.20×10^{-5}	1.40×10^{-4}
125	60	M	3.37×10^{-2}	2.79×10^{-5}	35.90×10^{-5}	1.01×10^{-4}
125	60	F	3.68×10^{-2}	4.38×10^{-5}	44.43×10^{-5}	1.68×10^{-4}
125	30	M	3.67×10^{-2}	3.35×10^{-5}	25.53×10^{-5}	1.08×10^{-4}
125	30	F	4.10×10^{-2}	4.27×10^{-5}	36.81×10^{-5}	1.64×10^{-4}
Control (ppm)						
0	90	M	3.31×10^{-2}	2.18×10^{-2}	5.80×10^{-5}	0.98×10^{-4}
0	90	F	3.60×10^{-2}	5.23×10^{-2}	8.81×10^{-5}	2.33×10^{-4}
0	60	M	3.79×10^{-2}	2.22×10^{-2}	6.42×10^{-5}	1.15×10^{-4}
0	60	F	3.82×10^{-2}	6.19×10^{-2}	8.59×10^{-5}	2.40×10^{-4}
0	30	M	4.22×10^{-2}	2.65×10^{-2}	6.70×10^{-5}	1.26×10^{-4}
0	30	F	4.43×10^{-2}	5.13×10^{-2}	7.14×10^{-5}	2.58×10^{-4}

TABLE 12. ORGAN WEIGHT: BRAIN WEIGHT RATIO

DDT (ppm)	Days on study	Sex	Ovary (paired, g)	Testicle (paired, g)	Pituitary (mg)	Thyroid (paired, g)	Adrenal (paired, mg)
625	90	M		2.53	5.61×10^{-3}	2.68×10^{-2}	2.26×10^{-2}
625	90	F	4.70×10^{-2}		7.99×10^{-3}	2.77×10^{-2}	2.60×10^{-2}
125	90	M		2.52	5.27×10^{-3}	1.62×10^{-2}	2.35×10^{-2}
125	90	F	5.13×10^{-2}		7.08×10^{-3}	1.31×10^{-2}	2.88×10^{-2}
25	90	M		2.59	5.04×10^{-3}	1.43×10^{-2}	2.49×10^{-2}
25	90	F	5.10×10^{-2}		7.72×10^{-3}	1.06×10^{-2}	3.13×10^{-2}
5	90	M		2.58	5.36×10^{-3}	1.25×10^{-2}	2.38×10^{-2}
5	90	F	5.67×10^{-2}		7.52×10^{-3}	1.00×10^{-2}	3.37×10^{-2}
1	90	M		2.50	4.79×10^{-3}	1.35×10^{-2}	2.44×10^{-2}
1	90	F	5.51×10^{-2}		7.71×10^{-3}	1.11×10^{-2}	3.51×10^{-2}
0	90	M		2.73	5.50×10^{-3}	1.47×10^{-2}	2.47×10^{-2}
0	90	F	5.28×10^{-2}		6.09×10^{-3}	1.36×10^{-2}	3.61×10^{-2}
625	60	M		1.81	5.81×10^{-3}	3.28×10^{-2}	2.36×10^{-2}
625	60	F	4.92×10^{-2}		5.54×10^{-3}	2.31×10^{-2}	2.69×10^{-2}
125	60	M		2.30	6.85×10^{-3}	1.85×10^{-2}	2.79×10^{-2}
125	60	F	7.08×10^{-2}		6.54×10^{-3}	1.48×10^{-2}	3.41×10^{-2}
25	60	M		2.52	5.09×10^{-3}	1.69×10^{-2}	2.38×10^{-2}
25	60	F	5.15×10^{-2}		6.68×10^{-3}	1.22×10^{-2}	3.16×10^{-2}
5	60	M		2.56	4.41×10^{-3}	1.05×10^{-2}	2.44×10^{-2}
5	60	F	5.48×10^{-2}		5.95×10^{-3}	0.96×10^{-2}	3.37×10^{-2}
1	60	M		2.51	4.63×10^{-3}	1.36×10^{-2}	2.52×10^{-2}
1	60	F	5.66×10^{-2}		6.75×10^{-3}	1.19×10^{-2}	3.11×10^{-2}
0	60	M		2.38	4.89×10^{-3}	1.41×10^{-2}	2.53×10^{-2}
0	60	F	6.25×10^{-2}		6.60×10^{-3}	1.22×10^{-2}	3.44×10^{-2}
625	30	M		2.25	7.21×10^{-3}	1.72×10^{-2}	2.23×10^{-2}
625	30	F	5.23×10^{-2}		4.34×10^{-3}	1.71×10^{-2}	2.21×10^{-2}
125	30	M		2.17	5.53×10^{-3}	1.37×10^{-2}	2.42×10^{-2}
125	30	F	6.52×10^{-2}		5.96×10^{-3}	1.36×10^{-2}	3.27×10^{-2}
25	30	M		2.25	4.63×10^{-3}	1.34×10^{-2}	2.57×10^{-2}
25	30	F	6.38×10^{-2}		4.68×10^{-3}	1.22×10^{-2}	3.42×10^{-2}
5	30	M		2.20	4.52×10^{-3}	1.02×10^{-2}	2.52×10^{-2}
5	30	F	6.36×10^{-2}		5.66×10^{-3}	0.99×10^{-2}	3.15×10^{-2}
1	30	M		2.06	4.01×10^{-3}	1.01×10^{-2}	2.36×10^{-2}
1	30	F	6.82×10^{-2}		4.31×10^{-3}	0.83×10^{-2}	3.43×10^{-2}
0	30	M		2.21	5.01×10^{-3}	1.26×10^{-2}	2.38×10^{-2}
0	30	F	6.69×10^{-2}		6.36×10^{-3}	0.88×10^{-2}	3.19×10^{-2}

TABLE 12. (Continued)

(ppm)	Days on Study	Sex	Heart (g)	Spleen (g)	St. Kidney (g)	Liver (g)
625	90	M	4.25×10^{-1}	1.57×10^{-1}	4.67×10^{-1}	4.20
625	90	F	3.51×10^{-1}	1.44×10^{-1}	3.89×10^{-1}	3.92
125	90	F	4.70×10^{-1}	4.06×10^{-1}	6.22×10^{-1}	9.30
125	90	F	4.88×10^{-1}	2.97×10^{-1}	3.12×10^{-1}	3.40
25	90	M	6.87×10^{-1}	6.10×10^{-1}	7.32×10^{-1}	8.56
25	90	F	5.07×10^{-1}	2.76×10^{-1}	3.27×10^{-1}	3.71
5	90	M	6.83×10^{-1}	5.29×10^{-1}	7.25×10^{-1}	8.10
5	90	F	4.78×10^{-1}	2.83×10^{-1}	3.32×10^{-1}	3.68
1	90	M	6.78×10^{-1}	3.89×10^{-1}	7.57×10^{-1}	8.80
1	90	F	4.66×10^{-1}	2.88×10^{-1}	3.21×10^{-1}	3.86
0	90	M	6.88×10^{-1}	4.32×10^{-1}	7.81×10^{-1}	8.35
0	90	F	5.08×10^{-1}	3.02×10^{-1}	3.51×10^{-1}	3.57
625	60	M	4.38×10^{-1}	1.76×10^{-1}	4.92×10^{-1}	4.56
625	60	F	3.45×10^{-1}	1.26×10^{-1}	4.07×10^{-1}	4.00
125	60	M	6.87×10^{-1}	3.77×10^{-1}	7.33×10^{-1}	8.71
125	60	F	5.11×10^{-1}	2.89×10^{-1}	3.89×10^{-1}	3.47
25	60	M	6.76×10^{-1}	4.91×10^{-1}	8.03×10^{-1}	10.20
25	60	F	4.69×10^{-1}	2.83×10^{-1}	3.21×10^{-1}	3.58
5	60	M	7.32×10^{-1}	4.30×10^{-1}	8.44×10^{-1}	9.14
5	60	F	4.88×10^{-1}	2.87×10^{-1}	3.08×10^{-1}	3.60
1	60	M	6.47×10^{-1}	3.61×10^{-1}	7.81×10^{-1}	8.60
1	60	F	4.56×10^{-1}	3.01×10^{-1}	3.37×10^{-1}	3.17
0	60	M	6.54×10^{-1}	3.59×10^{-1}	7.93×10^{-1}	8.35
0	60	F	4.73×10^{-1}	2.94×10^{-1}	3.30×10^{-1}	3.43
625	30	M	3.57×10^{-1}	1.86×10^{-1}	4.67×10^{-1}	4.90
625	30	F	3.06×10^{-1}	1.64×10^{-1}	3.81×10^{-1}	4.71
125	30	M	5.59×10^{-1}	3.94×10^{-1}	6.72×10^{-1}	8.37
125	30	F	4.65×10^{-1}	2.87×10^{-1}	3.03×10^{-1}	3.21
25	30	M	6.14×10^{-1}	4.21×10^{-1}	6.87×10^{-1}	7.91
25	30	F	4.59×10^{-1}	3.01×10^{-1}	3.11×10^{-1}	3.44
5	30	M	5.02×10^{-1}	3.02×10^{-1}	6.73×10^{-1}	6.17
5	30	F	4.39×10^{-1}	2.97×10^{-1}	4.70×10^{-1}	5.02
1	30	M	6.01×10^{-1}	3.76×10^{-1}	6.53×10^{-1}	7.38
1	30	F	4.13×10^{-1}	2.82×10^{-1}	4.31×10^{-1}	4.83
0	30	M	6.43×10^{-1}	4.00×10^{-1}	7.25×10^{-1}	7.97
0	30	F	4.76×10^{-1}	2.45×10^{-1}	4.87×10^{-1}	5.49

TABLE 12. (Continued)

Amitrole (ppm)	Days on Study	Sex	Heart (g)	Spleen (g)	Rt. Kidney (g)	Liver (g)
50	90	M	6.44×10^{-1}	3.99×10^{-1}	7.45×10^{-1}	8.59
50	90	F	4.69×10^{-1}	3.29×10^{-1}	5.35×10^{-1}	5.53
50	60	M	6.23×10^{-1}	3.67×10^{-1}	7.74×10^{-1}	8.52
50	60	F	4.92×10^{-1}	3.06×10^{-1}	5.35×10^{-1}	5.62
50	30	M	4.70×10^{-1}	2.89×10^{-1}	5.79×10^{-1}	7.29
50	30	F	4.17×10^{-1}	3.12×10^{-1}	4.96×10^{-1}	6.22
PTU						
125	90	M	3.82×10^{-1}	1.33×10^{-1}	4.14×10^{-1}	4.54
125	90	F	3.03×10^{-1}	1.10×10^{-1}	3.60×10^{-1}	3.69
125	60	M	3.81×10^{-1}	1.83×10^{-1}	4.88×10^{-1}	4.97
125	60	F	3.44×10^{-1}	1.58×10^{-1}	3.82×10^{-1}	4.15
125	30	M	3.36×10^{-1}	1.73×10^{-1}	4.34×10^{-1}	4.45
125	30	F	3.06×10^{-1}	1.43×10^{-1}	3.55×10^{-1}	4.04
Control						
0	90	M	6.68×10^{-1}	4.32×10^{-1}	7.81×10^{-1}	8.35
0	90	F	5.05×10^{-1}	3.02×10^{-1}	5.51×10^{-1}	5.57
0	60	M	6.54×10^{-1}	3.59×10^{-1}	7.93×10^{-1}	8.35
0	60	F	4.73×10^{-1}	2.94×10^{-1}	5.50×10^{-1}	5.43
0	30	M	6.41×10^{-1}	4.00×10^{-1}	7.25×10^{-1}	7.97
0	30	F	4.76×10^{-1}	2.95×10^{-1}	4.76×10^{-1}	5.49

TABLE 12. (Continued)

Anticore (μm)	Days on Study	Sex	Ovary (paired; g)	Testicle (paired; g)	Prostate (mg)	Thyroid (paired; g)	Adrenal (paired; mg)
50	90	M	—	2.58	6.20×10^{-3}	3.23×10^{-2}	2.40×10^{-2}
50	90	F	5.38×10^{-2}	—	9.23×10^{-3}	2.20×10^{-2}	3.22×10^{-2}
50	60	M	—	2.47	5.12×10^{-3}	1.79×10^{-2}	2.20×10^{-2}
50	60	F	5.50×10^{-2}	—	7.79×10^{-3}	1.30×10^{-2}	1.59×10^{-2}
50	30	M	—	2.17	4.13×10^{-3}	3.80×10^{-2}	1.88×10^{-2}
50	30	F	7.79×10^{-2}	—	4.42×10^{-3}	3.13×10^{-2}	3.47×10^{-2}
PVE							
125	90	M	—	2.42	4.39×10^{-3}	6.14×10^{-2}	1.55×10^{-2}
125	90	F	4.17×10^{-2}	—	5.56×10^{-3}	4.86×10^{-2}	1.50×10^{-2}
125	60	M	—	2.52	4.11×10^{-3}	5.30×10^{-2}	1.49×10^{-2}
125	60	F	5.06×10^{-2}	—	4.94×10^{-3}	5.01×10^{-2}	1.90×10^{-2}
125	30	M	—	2.14	4.05×10^{-3}	3.09×10^{-2}	1.30×10^{-2}
125	30	F	5.32×10^{-2}	—	4.21×10^{-3}	3.64×10^{-2}	1.67×10^{-2}
Control							
0	90	M	—	2.73	5.30×10^{-3}	1.47×10^{-2}	2.47×10^{-2}
0	90	F	5.51×10^{-2}	—	8.09×10^{-3}	1.36×10^{-2}	3.41×10^{-2}
0	60	M	—	2.38	4.80×10^{-3}	1.41×10^{-2}	2.53×10^{-2}
0	60	F	6.21×10^{-2}	—	8.80×10^{-3}	1.22×10^{-2}	3.41×10^{-2}
0	30	M	—	2.21	5.01×10^{-3}	1.26×10^{-2}	2.38×10^{-2}
0	30	F	6.65×10^{-2}	—	6.36×10^{-3}	0.89×10^{-2}	3.19×10^{-2}

TABLE 13. ANATOMICAL CHANGES OBSERVED FOR LIVER, SPLEEN AND THYROID.

Tissue Change	Days on Study	Sex	PPE	Antinucle	ESR					Control
					625	125	25	5	1	
Enlarged Thyroids; Rat	30	M	10	10	10	0	0	0	0	0
	30	F	10	10	5	2	0	0	0	0
Thyroids Normal Size but Rat	30	M	0	0	0	0	3	0	0	0
	30	F	0	0	0	0	2	0	0	0
Centrilobular Congestion; Liver	30	M	0	0	0	5	0	0	0	0
	30	F	0	0	0	0	0	0	0	0
Aplasia	30	M	0	0	0	0	0	0	0	0
	30	F	0	0	4	0	0	0	0	0
Small Adrenals	30	M	0	0	0	0	0	0	0	0
	30	F	0	1	0	0	0	0	0	0
Enlarged Thyroids; Rat	60	M	10	5	5	6	1	2	0	0
	60	F	10	2	9	1	0	7	0	0
Centrilobular Congestion; Liver	60	M	0	2	0	2	3	2	0	1
	60	F	0	0	0	0	0	0	0	0
Aplasia	60	M	0	2	5	0	0	0	0	0
	60	F	0	0	0	0	0	0	0	0
Enlarged Thyroids; Rat	90	M	10	10	0	10	0	0	0	0
	90	F	10	5	0	6	0	0	0	0
Aplasia	90	M	0	0	0	0	0	0	0	0
	90	F	0	0	4	0	0	0	0	0
Centrilobular Congestion; Liver	90	M	0	1	0	9	1	3	0	1
	90	F	0	2	0	0	1	0	2	0
Small Adrenals	90	M	0	0	0	0	0	0	0	0
	90	F	0	0	0	0	0	0	0	0
Adenocarcinoma of Salivary Gland	90	M	0	0	0	0	0	0	0	0
	90	F	1	0	0	0	0	0	0	0

Presented as % of number of animals with the indicated tissue change, out of the 10 animals evaluated. Relative male and eleven female control rats were evaluated from 30 day group. Twelve male and twelve female rats were evaluated from the 60 and 90 day control groups.

Relative male rats and one female rat from the 625 ppm 60 day group died prior to the end of the study. Therefore, the values for this one group are based on the evaluation of five male and one female rat. Twelve female rats died prior to the end of the 90 days. Therefore, the values for females in this one group are based on eight rats.

TABLE 14. GRADING OF DEGREE OF HYPERPLASIA FROM MICROSCOPIC APPEARANCE OF THE THYROID GLAND

Grade of Hyperplasia	Description of Change in Morphology
0	Completely normal appearing gland.
+1	Very slightly altered lining cells and scalloping of colloid.
1	Distinct hyperplasia or hypertrophy of lining cells and a moderate reduction of colloid.
+2	Hyperplastic change of lining cells and folding of follicular wall with a moderate reduction of colloid.
2	Moderate hyperplasia of lining cells, increase in apparent number of microfollicular follicles reducing apparent colloid to less than fifty percent of normal.
+3	More extensive microfollicular pattern but still retaining approximately twenty-five percent colloid.
3	Marked hyperplasia of lining cells with virtually all microfollicular follicles and nearly complete absence of colloid.

TABLE 15. THYROID HYPERPLASIA OBSERVED IN ETU TEST ANIMALS

Degree of Hyperplasia	Days on Study	PTU		Amitrole		ETU			
		125	50	625	125	25	5	1	0
0	30	0	0	0	0	0	1	0	1
=1	30	0	0	0	0	9	6	7	9
1	30	0	0	2	18	11	13	13	10
=2	30	0	0	4	1	0	0	0	0
2	30	8	0	12	1	0	0	0	0
=3	30	3	5	2	0	0	0	0	0
3	30	9	13	0	0	0	0	0	0
0	60	0	0	0	1	7	4	1	5
=1	60	0	4	0	3	2	7	9	10
1	60	0	5	2	7	0	9	10	9
=2	60	0	8	2	5	7	0	0	0
2	60	0	1	10	2	4	0	0	0
=3	60	17	0	0	0	0	0	0	0
3	60	3	0	0	2	0	0	0	0
0	90	0	0	0	1	3	6	6	12
=1	90	0	5	0	0	8	8	6	9
1	90	0	14	1	14	9	6	8	3
=2	90	0	0	1	1	0	0	0	0
2	90	1	1	12	1	0	0	0	0
=3	90	10	0	1	0	0	0	0	0
3	90	9	0	1	1	0	0	0	0

TABLE 16. CHANGES IN THYROID MORPHOLOGY IN RATS WHICH
INGESTED 625 PPM ETU FOR NINETY DAYS*

Rat Number	Sex	Solid Adenomas	Cystic Adenomas	Adenomatous Changes	Cyst-like Follicles
560	M	1	0	0	0
561	M	1	2	2	0
562	M	1	1	0	0
563	M	0	0	1	0
564	M	1	0	2	0
565	M	0	0	0	1
566	M	0	0	0	0
567	M	2	0	0	0
568	M	0	0	0	1
569	M	0	0	0	0
570	F	Died			
571	F	Died			
572	F	2	0	1	0
573	F	0	0	0	1
574	F	0	0	0	0
575	F	0	0	1	0
576	F	0	0	0	0
577	F	0	0	0	1
578	F	1	0	0	0
579	F	0	0	0	0

*Thyroids examined by serial sectioning.